

Exhibit 1

The American College of
Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS



FREQUENTLY ASKED QUESTIONS

FAQ096

GYNECOLOGIC PROBLEMS

Ovarian Cancer

- What is cancer?
- What is ovarian cancer?
- What are the types of ovarian cancer?
- What are the risk factors for ovarian cancer?
- What screening tests are available for ovarian cancer?
- What are the symptoms of ovarian cancer?
- How is ovarian cancer diagnosed?
- How is ovarian cancer treated?
- What type of follow-up is needed after treatment?
- How can I reduce my risk of ovarian cancer?
- What should I know if I am at high risk of ovarian cancer?
- Glossary

What is cancer?

Normal cells in the body grow, divide, and are replaced on a routine basis. Sometimes, cells divide abnormally and begin to grow out of control. These cells may form growths or tumors.

Tumors can be benign (not cancer) or malignant (cancer). Benign tumors do not spread to other body tissues. Malignant tumors can invade and destroy nearby healthy tissues and organs. Cancer cells also can spread to other parts of the body and form new cancerous areas.

What is ovarian cancer?

Ovarian cancer is cancer that affects one or both **ovaries**. Ovarian cancer is not common. But because ovarian cancer often goes undetected until it is in an advanced stage, it is the number one cause of deaths from gynecologic cancer in the United States.

What are the types of ovarian cancer?

Ovarian cancer can develop on the surface of the ovary or from tissues inside the ovary. There are three main types. The type that develops on the surface of the ovary, epithelial ovarian cancer, is the most common type. About 90% of cases of ovarian cancer involve epithelial tumors. This FAQ discusses epithelial ovarian cancer.

What are the risk factors for ovarian cancer?

Certain risk factors are associated with epithelial ovarian cancer. The following factors have been shown to increase a woman's risk of getting this type of cancer:

- Age older than 55 years
- Family history of breast cancer, ovarian cancer, colon cancer, or endometrial cancer (cancer of the lining of the **uterus**)
- Personal history of breast cancer
- **Mutations in *BRCA1* and *BRCA2* genes**
- Never having had children

- Infertility
- **Endometriosis**
- **Lynch Syndrome**

What screening tests are available for ovarian cancer?

A screening test is a test that is done when no symptoms are present. Examples of screening tests are **colonoscopy** for colorectal cancer and the **Pap test** for cervical cancer. Currently, there is no screening test for ovarian cancer. You should be alert to any changes in your body and discuss them with your **obstetrician–gynecologist (ob-gyn)** or health care professional. The earlier that ovarian cancer is diagnosed, the more likely that treatment will be successful.

What are the symptoms of ovarian cancer?

If you have any of the following symptoms, especially if you have them for more than 12 days per month, contact your ob-gyn or other health care professional:

- Bloating or an increase in abdominal size
- Pelvic or abdominal pain
- Difficulty eating or feeling full quickly
- Urinary symptoms (frequency and urgency)

Others symptoms can include vaginal bleeding, especially after **menopause**, and a change in bowel habits. Having these symptoms does not mean that you have ovarian cancer, but it is a good idea to find out what is causing them.

How is ovarian cancer diagnosed?

If you have frequent or persistent symptoms of ovarian cancer, you may have a physical exam, including a **pelvic exam**. An imaging test of the ovaries, such as a **transvaginal ultrasound exam**, may be done. If a growth is found on an ovary, your ob-gyn may order a blood test to measure your **CA 125** level. CA 125 sometimes is increased in women with ovarian cancer. Results of these tests are used to assess the likelihood that the growth is cancer. Test results also will guide the next steps in evaluation.

How is ovarian cancer treated?

If a woman is thought to have ovarian cancer, surgery usually is recommended to remove the uterus, ovaries, and **fallopian tubes**. **Lymph nodes** and tissues in the pelvis and abdomen are checked for cancer and may be removed as well. In some cases, only the ovary with cancer may be removed. Chemotherapy after surgery is recommended for most cases of ovarian cancer. **Chemotherapy** is the use of drugs that kill cancer cells. In some cases, chemotherapy may be recommended before surgery.

What type of follow-up is needed after treatment?

Women treated for ovarian cancer need to have regular checkups to make certain that the cancer has not come back. A checkup after cancer treatment usually includes a review of symptoms and a physical exam. The checkup also may include a CA 125 test. Imaging tests are not routinely done but may be recommended. These may include ultrasound, chest X-ray, **magnetic resonance imaging (MRI)**, or **computed tomography (CT)**.

How can I reduce my risk of ovarian cancer?

Combined hormonal birth control pills (those that contain estrogen and **progestin**) may reduce the risk of ovarian cancer. The longer a woman takes the pill, the more the risk is reduced—for every 5 years on the pill, a woman reduces her risk by about 20%. This benefit needs to be balanced against the risks of using the pill. The pill is safe for most women, but it is associated with a small increased risk of **deep vein thrombosis (DVT)**, heart attack, and stroke.

Current theories suggest that some types of ovarian cancer may start in the fallopian tubes. If you need to have your uterus removed or you have chosen sterilization as a permanent method of birth control, you may want to ask your ob-gyn or other health care professional about having your fallopian tubes removed. This operation is called a **salpingectomy**. In this procedure, only the fallopian tubes are removed. The ovaries are left in place. A salpingectomy may help reduce the risk of future ovarian cancer.

What should I know if I am at high risk of ovarian cancer?

For women at high risk of ovarian cancer, such as women with **BRCA1** or **BRCA2** mutations, periodic tests to check for ovarian cancer may be recommended. These tests may include transvaginal ultrasound exam to look for changes in the ovaries and a CA 125 test.

Risk-reducing salpingo-oophorectomy also is an option. This is the removal of the fallopian tubes and the ovaries in a woman who does not have cancer. It is recommended for women with **BRCA1** or **BRCA2** mutations by age 40 years or when childbearing is complete. It also may be recommended for women with Lynch syndrome. This operation reduces the risk of ovarian cancer.

Glossary

BRCA1 and BRCA2: Genes that function in the control of cell growth. Changes in these genes have been linked to an increased risk of breast cancer and ovarian cancer.

CA 125: A substance in the blood that may increase in the presence of some cancerous tumors.

Chemotherapy: Treatment of cancer with drugs.

Colonoscopy: An exam of the entire colon using a small, lighted instrument.

Computed Tomography (CT): A type of X-ray procedure that shows internal organs and structures in cross section.

Deep Vein Thrombosis (DVT): A condition in which a blood clot forms in veins in the leg or other areas of the body.

Endometriosis: A condition in which tissue that lines the uterus is found outside of the uterus, usually on the ovaries, fallopian tubes, and other pelvic structures.

Fallopian Tubes: Tubes through which an egg travels from the ovary to the uterus.

Genes: Segments of DNA that contain instructions for the development of a person's physical traits and control of processes in the body. They are the basic units of heredity and can be passed down from parent to child.

Lymph Nodes: Small clusters of special tissue located throughout the body that filter lymph, a nearly colorless liquid that bathes body cells. Lymph nodes are connected to each other by lymph vessels. Together, these structures make up the lymphatic system.

Lynch Syndrome: A genetic condition that increases a person's risk of several types of cancer, including colon cancer, ovarian cancer, and endometrial cancer.

Magnetic Resonance Imaging (MRI): A method of viewing internal organs and structures by using a strong magnetic field and sound waves.

Menopause: The time in a woman's life when menstruation stops; defined as the absence of menstrual periods for 1 year.

Mutations: Permanent changes in a gene that can be passed on from parent to child.

Obstetrician–Gynecologist (Ob-Gyn): A physician with special skills, training, and education in women's health.

Ovarian Cancer: Cancer that affects one or both of the ovaries.

Ovaries: The paired organs in the female reproductive system that contain the eggs released at ovulation and that produce hormones.

Pap Test: A test in which cells are taken from the cervix and vagina and examined under a microscope.

Pelvic Exam: A physical examination of a woman's reproductive organs.

Progestin: A synthetic form of progesterone that is similar to the hormone produced naturally by the body.

Risk-Reducing Salpingo-oophorectomy: Surgical removal of healthy fallopian tubes and ovaries.

Salpingectomy: Removal of one or both of the fallopian tubes.

Transvaginal Ultrasound: A type of ultrasound in which a device specially designed to be placed in the vagina is used.

Uterus: A muscular organ located in the female pelvis that contains and nourishes the developing fetus during pregnancy.

If you have further questions, contact your obstetrician–gynecologist.

FAQ096: Designed as an aid to patients, this document sets forth current information and opinions related to women's health. The information does not dictate an exclusive course of treatment or procedure to be followed and should not be construed as excluding other acceptable methods of practice. Variations, taking into account the needs of the individual patient, resources, and limitations unique to the institution or type of practice, may be appropriate.

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Exhibit 2



The American College of
Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS



Society of Gynecologic Oncology

ACOG PRACTICE BULLETIN

Clinical Management Guidelines for Obstetrician–Gynecologists

NUMBER 182, SEPTEMBER 2017

(Replaces Practice Bulletin Number 103, April 2009)

Committee on Practice Bulletins–Gynecology, Committee on Genetics, Society of Gynecologic Oncology. This Practice Bulletin was developed by the American College of Obstetrician and Gynecologists' Committee on Practice Bulletins–Gynecology and Committee on Genetics in collaboration with Susan C. Modesitt, MD, and Karen Lu, MD, and by the Society of Gynecologic Oncology in collaboration with Lee-may Chen, MD, and C. Bethan Powell, MD.

Hereditary Breast and Ovarian Cancer Syndrome

Hereditary breast and ovarian cancer syndrome is an inherited cancer-susceptibility syndrome characterized by multiple family members with breast cancer, ovarian cancer, or both. Based on the contemporary understanding of the origins and management of ovarian cancer and for simplicity in this document, ovarian cancer also refers to fallopian tube cancer and primary peritoneal cancer. Clinical genetic testing for gene mutations allows more precise identification of those women who are at an increased risk of inherited breast cancer and ovarian cancer. For these individuals, screening and prevention strategies can be instituted to reduce their risks. Obstetrician–gynecologists play an important role in the identification and management of women with hereditary breast and ovarian cancer syndrome. If an obstetrician–gynecologist or other gynecologic care provider does not have the necessary knowledge or expertise in cancer genetics to counsel a patient appropriately, referral to a genetic counselor, gynecologic or medical oncologist, or other genetics specialist should be considered (1). More genes are being discovered that impart varying risks of breast cancer, ovarian cancer, and other types of cancer, and new technologies are being developed for genetic testing. This Practice Bulletin focuses on the primary genetic mutations associated with hereditary breast and ovarian cancer syndrome, BRCA1 and BRCA2, but also will briefly discuss some of the other genes that have been implicated.

Background

BRCA1 and BRCA2

Germline mutations in the *BRCA1* and *BRCA2* (*BRCA*) genes account for most cases of hereditary breast and ovarian cancer syndrome. Approximately 9–24% of cases of epithelial ovarian cancer (2–5) and approximately 4.5% of cases of breast cancer (6) are due to germline mutations in *BRCA1* and *BRCA2*. *BRCA1* is found on chromosome 17 and *BRCA2* is on chromosome 13 (7, 8). Both *BRCA* genes are tumor suppressor genes that encode proteins that function in the DNA repair process (9, 10). Individuals with hereditary breast and ovarian cancer syndrome inherit one defective allele in *BRCA1* or *BRCA2* from their father or mother, but they

have a second, functional allele. If the second allele becomes nonfunctional as a result of a somatic mutation, cancer can develop. This is called the “two-hit hypothesis” (11).

Founder BRCA Mutations

In the general population, it is estimated that approximately 1 in 300 to 1 in 800 individuals carry a mutation in *BRCA1* or *BRCA2* (12). In certain populations founded by a small ancestral group, a specific mutation in *BRCA1* or *BRCA2* may occur more frequently, and is often referred to as a founder mutation. These founder mutations in *BRCA1* and *BRCA2* have been identified in Ashkenazi (Central and Eastern European) Jews, French Canadians, and Icelanders, among other groups.

Particularly relevant to clinical practice in the United States, an estimated 1 in 40 Ashkenazi Jews carries one of three founder mutations in *BRCA1* or *BRCA2* (13, 14). *BRCA1* and *BRCA2* mutations also have been found in individuals of diverse ethnic backgrounds, including Hispanic, African American, and Asian (15, 16).

Other Hereditary Breast and Ovarian Cancer Syndrome Mutations

In addition to *BRCA1* and *BRCA2*, other genes are implicated in hereditary breast and ovarian cancer syndrome. These other genes may account for up to 25% of hereditary ovarian cancer risk (4). Although a comprehensive review of each individual gene is outside the scope of this Practice Bulletin, patients found to have pathogenic variants in other implicated genes (Table 1) may benefit from risk-reduction management strategies for breast cancer, ovarian cancer, or both. The National Comprehensive Cancer Network guidelines are updated annually and may serve as a contemporary reference (17).

Risk of Breast Cancer

The estimated risk of breast cancer in individuals with a *BRCA1* or *BRCA2* mutation is 45–85% by age 70 years (18–20). A meta-analysis of 10 studies that included a

total of 1,641 carriers from multiple countries calculated a mean cumulative risk of breast cancer of 57% for *BRCA1* mutation carriers and 49% for *BRCA2* carriers (21). For *BRCA* mutation carriers with breast cancer, the 10-year actuarial risk of developing subsequent ovarian cancer is 12.7% for *BRCA1* and 6.8% for *BRCA2* (22).

The type of breast cancer also may vary based on *BRCA* mutation type. For example, a woman with triple-negative breast cancer (ie, estrogen-receptor negative, progesterone negative, and *ERBB2*-negative [also known as *HER2/neu* negative]) has a 10–39% chance of having a *BRCA1* or *BRCA2* mutation, with *BRCA1* being more likely (23). This is in contrast to the types of breast cancer diagnosed in women with *BRCA2* mutations, which are more commonly estrogen-receptor and progesterone-receptor positive (24, 25).

Risk of Ovarian Cancer

For a woman with a *BRCA1* mutation, the risk of ovarian cancer (including fallopian tube cancer and primary peritoneal cancer) is approximately 39–46% by age 70 years (18–21). For a woman with a *BRCA2* mutation, the risk of ovarian cancer by age 70 years is 10–27% (18–21). Ovarian cancer that is associated with *BRCA1* and *BRCA2* mutations usually is high grade and has a

Table 1. Genetic Mutations Associated With Hereditary Breast and Ovarian Cancer Syndrome

Gene	Breast Cancer Risk	Ovarian Cancer Risk*	Other Cancer Risk
<i>ATM</i>	Increased	No increased risk	Insufficient evidence
<i>BRCA1</i>	Increased	Increased	Prostate
<i>BRCA2</i>	Increased	Increased	Melanoma, pancreas, prostate
<i>BRIP1</i>	No increased risk	Increased	Insufficient evidence
<i>CDH1</i>	Increased	No increased risk	Stomach
<i>CHEK2</i>	Increased	No increased risk	Colon
Lynch Syndrome Genes: <i>MSH2</i> , <i>MLH1</i> , <i>MSH6</i> , <i>PMS2</i> , and <i>EPCAM</i>	Insufficient evidence	Increased	Colon, uterine, renal pelvis, small bowel, and others
<i>PALB2</i>	Increased	No increased risk	Unknown
<i>PTEN</i>	Increased	No increased risk	Cowden Syndrome
<i>RAD51C</i>	No increased risk	Increased	Unknown
<i>RAD51D</i>	No increased risk	Increased	Unknown
<i>STK11</i>	Increased risk	Increased risk of sex cord stromal tumors	Peutz-Jehger Syndrome
<i>TP53</i>	Increased	No increased risk	Li-Fraumeni Syndrome

*Includes fallopian tube cancer and primary peritoneal cancer.

Data from National Comprehensive Cancer Network. Genetic/familial high risk assessment: breast and ovarian. Version 2.2017. NCCN Clinical Practice Guidelines in Oncology. Fort Washington (PA): NCCN; 2016. Available at: https://www.nccn.org/professionals/physician_gls/pdf/genetics_screening.pdf.

distinct histologic phenotype that is predominantly serous or endometrioid. A woman with high-grade ovarian cancer has a 9–24% chance of carrying a germline *BRCA1* or *BRCA2* mutation. (2–5). Mucinous cancer and borderline ovarian tumors do not appear to be part of the *BRCA*-related tumor spectrum (26–28).

There are growing data to support the fallopian tube as the site of origin for a large percentage of cases of *BRCA*-associated, high-grade serous cancer (29, 30). Multiple pathologic studies of the fallopian tubes and ovaries of women with *BRCA1* and *BRCA2* mutations who underwent risk-reducing salpingo-oophorectomy have identified cases of early microscopic high-grade cancer that were located predominantly in the fallopian tube as well as cases of serous tubal intraepithelial carcinoma (31, 32). Findings of these occult lesions are seen more frequently when risk-reducing salpingo-oophorectomy is delayed until a later age, and women with these findings have a higher risk of subsequent peritoneal carcinoma (33, 34).

Risk of Other Types of Cancer

Patients with *BRCA* mutations also carry other cancer risks (albeit smaller than their risk of breast and ovarian cancer), including prostate cancer, pancreatic cancer, melanoma, and potentially uterine cancer (35, 36). *BRCA2* mutation carriers have a threefold increased risk and up to a 7% lifetime risk of pancreatic cancer. Additionally, *BRCA2* mutation carriers have an increased risk of melanoma, and male carriers have an increased prostate cancer risk (17). There is ongoing investigation regarding the potential significant (but small) increased risk of uterine cancer. Some studies to date have not shown increased risk, whereas others have shown increased risk, specifically of high-grade histology in *BRCA1* mutation carriers (eg, uterine papillary serous cancer) (37, 38).

Clinical Considerations and Recommendations

► *Who are candidates for genetic counseling for hereditary breast and ovarian cancer syndrome?*

Genetic counseling is recommended for all women with ovarian epithelial cancer (this includes fallopian tube cancer or primary peritoneal cancer) and for individuals who have a personal or family history of breast cancer or ovarian cancer. Evaluating a patient's risk of hereditary breast and ovarian cancer syndrome should be a routine part of obstetric and gynecologic practice. Initial risk

evaluation should include a personal medical history and family history. At minimum, this evaluation should include a personal cancer history and a family cancer history that includes first-degree and second-degree relatives from the paternal and maternal lineages, a description of the type of primary cancer, the age of onset, and the lineage (paternal versus maternal) of the family member. In addition, a patient's ethnic background can influence her genetic risk; thus, understanding this background is relevant in assessing a patient's predisposition to a hereditary breast and ovarian cancer syndrome (39).

The American College of Obstetricians and Gynecologists (39) and the American Society of Clinical Oncologists (40) have published guidance on the elements to be included as part of a cancer family history. When evaluating a family history, it is important to remember that predisposing genes for breast cancer and ovarian cancer, fallopian tube cancer, and primary peritoneal cancer can be transmitted through the father as well as the mother. Therefore, paternal family history should be obtained. Adoption can limit interpretation of a pedigree, and hysterectomy and oophorectomy at a young age in multiple family members can mask a hereditary gynecologic cancer predisposition. Also, the ability to assess breast cancer risk is limited in families with few female members. Women from high-risk groups with a higher rate of *BRCA* mutations (eg, Ashkenazi Jews, French Canadians, and Icelanders) should have a low threshold for referral for genetic counseling.

Guidelines from the American College of Medical Genetics and Genomics (41), the National Society of Genetic Counselors (41), the National Comprehensive Care Network (17), and the Society of Gynecologic Oncology (42) provide specific clinical criteria to assist health care providers in determining which patients would benefit from genetic counseling. The main criteria are similar across the guidelines and are listed in [Box 1](#). Familial risk stratification models also may be used in initial risk screening for *BRCA*-related cancer. These brief risk tools are primarily intended for use by nongenetic specialists to guide patient referrals for more extensive genetic risk assessment and evaluation (43). Several models have been evaluated by the U.S. Preventive Services Task Force and the Agency for Healthcare Research and Quality, although there is insufficient evidence to recommend any particular risk model or a specific risk threshold for referral (43).

► *What issues should be addressed during genetic counseling?*

Genetic counseling is recommended before initiation of genetic testing and can be performed by an

Box 1. Criteria for Further Genetic Evaluation for Hereditary Breast and Ovarian Cancer ⇐

- Women affected with one or more of the following have an increased likelihood of having an inherited predisposition to breast* and ovarian, tubal, or peritoneal cancer and should receive genetic counseling and be offered genetic testing:
 - Epithelial ovarian, tubal, or peritoneal cancer
 - Breast cancer at age 45 years or less
 - Breast cancer and have a close relative[†] with breast cancer at age 50 years or less or close relative[†] with epithelial ovarian, tubal, or peritoneal cancer at any age
 - Breast cancer at age 50 years or less with a limited or unknown family history[‡]
 - Breast cancer and have two or more close relatives[†] with breast cancer at any age
 - Breast cancer and have two or more close relatives[†] with pancreatic cancer or aggressive prostate cancer (Gleason score equal to or greater than 7)
 - Two breast cancer primaries, with the first diagnosed before age 50 years
 - Triple-negative breast cancer at age 60 years or less
 - Breast cancer and Ashkenazi Jewish ancestry at any age
 - Pancreatic cancer and have two or more close relatives[†] with breast cancer; ovarian, tubal, or peritoneal cancer; pancreatic cancer; or aggressive prostate cancer (Gleason score equal to or greater than 7)
- Women unaffected with cancer, but with one or more of the following have an increased likelihood of having an inherited predisposition to breast and ovarian, tubal, or peritoneal cancer and should receive genetic counseling and be offered genetic testing:
 - A first-degree or several close relatives[†] that meet one or more of the aforementioned criteria
 - A close relative[†] carrying a known *BRCA1* or *BRCA2* mutation[§]
 - A close relative[†] with male breast cancer

*Invasive and ductal carcinoma in situ breast cancer.

[†]Close relative is defined as first degree (parent, sibling, offspring), second degree (grandparent, grandchild, uncle, aunt, nephew, niece, half-sibling), or third degree (first cousin, great-grandparent or great-grandchild).

[‡]Limited family history includes fewer than two first-degree or second-degree female relatives surviving beyond age 45 years.

[§]Or carrying another known actionable deleterious mutation associated with hereditary breast and ovarian cancer syndrome.

Adapted with permission from Lancaster JM, Powell CB, Chen LM, Richardson DL. Society of Gynecologic Oncology statement on risk assessment for inherited gynecologic cancer predispositions. SGO Clinical Practice Committee [published erratum appears in Gynecol Oncol 2015;138:765]. *Gynecol Oncol* 2015;136:3–7.

obstetrician–gynecologist (or other gynecologic care provider) who has expertise in cancer genetics or by a genetic counselor. Pretest genetic counseling includes the following:

- Detailed pedigree (or kindred analysis)
- Risk assessment to determine eligibility for genetic testing and identification of candidates in the family to proceed with genetic testing
- An informed consent process, including patient education about the benefits, harms, limitations, and possible outcomes of genetic testing, as well as the practical and ethical issues associated with disclosure or nondisclosure of test results to family members.

Posttest counseling includes reporting and interpretation of the results and discussion of management options such as intensive screening and risk-reduction interventions.

Several online risk models are available to estimate a woman's risk of developing breast cancer, gynecologic cancer, or both, and to help identify women who are candidates for genetic testing, intensive cancer screening, and risk-reduction measures. These models include *BRCAPRO* (available at www4.utsouthwestern.edu/breasthealth/cagene/), Tyrer–Cuzick or IBIS (available at www.ems-trials.org/riskevaluator/), and BOADICEA (available at www.srl.cam.ac.uk/genepi/boadicea/boadicea_home.html) (44–46). Two other risk prediction models have been developed for ovarian cancer. They include inherited and noninherited risk factors such as family history of breast and ovarian cancer, age at menarche, oral contraceptive pill use, history of tubal ligation, age at menopause, and menopausal hormonal therapy use (47, 48).

The possible outcomes of any genetic testing should be discussed as part of pretest genetic counseling (Box 2). This includes the possibility of variants of uncertain significance, which are genetic abnormalities for which the clinical significance to the individual and family remain unclear. If providing genetic testing, practitioners should have a process to inform patients if a variant of uncertain significance is reclassified. Genetic counseling also may include discussion of possible psychologic, reproductive, and familial implications of test results. Potential adverse psychologic effects of genetic testing include increased breast cancer-related worry and anxiety for women with positive or uninformative test results (49). Patients may feel burdened and distressed about disclosure of test results to family members. Written materials may help individuals share information with relatives about their potential genetic risks. Because a positive test result may affect family

Box 2. Possible Outcomes of *BRCA* Mutation* Testing ⇐

- True positive—Indicates detection of a pathogenic *BRCA* variant in the individual.
- True negative—Indicates the absence of a pathogenic variant in an individual who has relatives with cancer and a known pathogenic *BRCA* variant in the family.
- Uninformative negative—Indicates the absence of a pathogenic variant in an individual; however, this negative test result is inconclusive because it can occur for several reasons:
 - Other family members have not been tested
 - The family carries a pathogenic *BRCA* variant, but it was not detected because of limitations of the test
 - The family carries a high-risk mutation in another gene
 - There is no high-risk mutation in the family
- Variant of uncertain clinical significance—Indicates the presence of an abnormality of the *BRCA* gene, but it is unknown whether the variant is associated with an increased risk of cancer.

*Or other known actionable deleterious mutation associated with hereditary breast and ovarian cancer syndrome.

Data from Nelson HD, Fu R, Goddard K, Mitchell JP, Okinaka-Hu L, Pappas M, et al. Risk assessment, genetic counseling, and genetic testing for *BRCA*-related cancer: systematic review to update the U.S. Preventive Services Task Force recommendation. Evidence Synthesis No. 101. AHRQ Publication No. 12-05164-EF-1. Rockville (MD): Agency for Healthcare Research and Quality; 2013.

members, all gynecologic care providers can have a role in advocating the education, referral, and testing of family members of affected individuals—otherwise known as “cascade” testing.

Genetic counseling also may include discussion of other potential implications of genetic testing, such as cost, privacy, and insurance coverage. Medicare and other insurance companies have written guidelines for covering the cost of genetic testing, and anyone ordering genetic testing will need to understand the various tests that are available as well as insurance coverage requirements. Another important aspect of genetic counseling is discussion of current legislation regarding genetic discrimination and the privacy of genetic information. The federal Genetic Information Nondiscrimination Act of 2008 protects individuals against health and employment discrimination based on genetic information (50). Many states also have laws that provide similar protection. These laws do not apply to other forms of insurance, which may include life or disability insurance.

Common clinical and ethical issues regarding genetic counseling and genetic testing in gynecologic care are presented and addressed in a case format in

the *Genetics Toolkit* (www.sgo.org/genetics/genetics-toolkit/), a collaborative effort of the Society of Gynecologic Oncology, the American College of Obstetricians and Gynecologists, the National Society of Genetic Counselors, Bright Pink, and Facing Our Risk of Cancer Empowered (FORCE). The American College of Obstetricians and Gynecologists’ genetics web page (www.acog.org/Genetics) and *Committee Opinion No. 693, Counseling About Genetic Testing and Communication of Genetic Test Results*, include additional guidance and information on the clinical and ethical issues related to genetic testing in gynecologic practice.

► What genetic testing approach should be offered?

Genetic testing is recommended when the results of a detailed risk assessment that is performed as part of genetic counseling suggest the presence of an inherited cancer syndrome for which specific genes have been identified and when the results of testing are likely to influence medical management (51). Genetic testing will not be appropriate for every patient referred for genetic counseling and not every patient who is offered genetic testing will choose to act on that recommendation.

The two main genetic testing options for hereditary breast and ovarian cancer syndrome are *BRCA* mutation testing and multigene panel testing that includes *BRCA* and other genetic mutations. The choice of testing strategy will depend on whether or not there is a known mutation in the family (49). If possible, any genetic testing should begin with the cancer-affected individual in the family, who may have early-onset breast cancer, ovarian cancer, or another *BRCA*-associated cancer (eg, pancreatic cancer, melanoma, or early-onset prostate cancer) because this will provide the best answer as to whether the familial cancer is due to a known genetic mutation. If that person cannot be tested, the closest cancer-affected relative to that person may be appropriate for testing, with the understanding that a negative genetic test result in this situation may be uninformative.

***BRCA* Mutation Testing**

BRCA mutation testing comprises single-site testing, targeted multisite mutation testing, comprehensive gene sequencing, and *BRCA* rearrangement testing (49). If a specific *BRCA* mutation is identified in an affected individual, a single-site test can be recommended for family members to look for that specific genetic mutation already identified (ie, “predictive testing”). For members of certain ethnic and geographic groups who are at risk of founder mutations, but who do not have a personal or family history of breast or ovarian cancer,

targeted multisite testing for common mutations can be performed and is less expensive than full sequence testing. Genetic testing has evolved over the years so patients who underwent *BRCA* genetic testing before the routine initiation of *BRCA* Rearrangement Testing, may need repeat testing or evaluation.

Multigene Panel Testing

Technologic advances in genetic sequencing have resulted in the ability to perform parallel sequencing of multiple genes more quickly and cost effectively than in the past. The goal of panel testing is to maximize finding an actionable genetic mutation (ie, findings likely to affect medical management) (Table 1). Multiple companies now offer genetic panel testing for cancer-related genes with combinations of genes that may be associated with specific types of cancer (eg, breast-ovarian, gynecologic, colon, pancreas, and kidney).

Multigene panel testing may be useful when more than one gene may be associated with an inherited cancer syndrome (17, 51) or when a patient has a personal or family history that is consistent with an inherited cancer susceptibility, but single-gene testing has not identified a pathogenic variant (17). Multigene panel tests should be offered by a health care provider with cancer genetics expertise and after genetic counseling and informed consent. Although mutations in *BRCA1* and *BRCA2* account for most cases of hereditary breast and ovarian cancer, other genes have been found to be associated with this hereditary syndrome (Table 1), and results showing mutations in such genes may affect patient counseling regarding screening and risk-reduction measures.

An important consideration for multigene panel testing is the increased complexity and uncertainty of the results and how this affects interpretation, patient counseling, and medical management. Because panel testing involves the simultaneous testing of multiple genes and can include genes that confer moderate or uncertain risk, there is an increased likelihood of finding variants of uncertain significance for which there are limited (or no) data on associated cancer risk to guide appropriate management (17). Health care providers who order these multigene panel tests should be prepared to guide their patients appropriately and contact them if variant classifications change.

► How should women with mutations in *BRCA1* or *BRCA2* be counseled to reduce the risk of ovarian cancer?

Current strategies to reduce the risk of developing ovarian cancer (including fallopian tube cancer) in women at

high risk with known deleterious *BRCA* mutations may include risk-reducing agents and surgery (17).

Screening

In women with *BRCA* mutations or who have a personal or family history of ovarian cancer, routine ovarian cancer screening with measurement of serum CA 125 level or transvaginal ultrasonography generally is not recommended (17). Transvaginal ultrasonography or measurement of serum CA 125 level may be reasonable for short-term surveillance in women at high risk of ovarian cancer starting at age 30–35 years until the time they choose to pursue risk-reducing bilateral salpingo-oophorectomy, which is the only proven intervention to reduce ovarian cancer-specific mortality (17). Available screening procedures (measurement of serum CA 125 level and transvaginal ultrasonography) have not been proved to decrease the mortality rate or increase the survival rate associated with ovarian cancer in high-risk populations (49).

The low prevalence of ovarian cancer and the high likelihood of a positive screening test result that leads to potentially unnecessary invasive surgical evaluation are current obstacles in ovarian cancer screening programs among women at inherited risk (52–54). The largest trial to date in high-risk women (United Kingdom Familial Ovarian Cancer Screening Study-UK-FOCSS, 2017) monitored women with CA 125 level screening (using the risk of ovarian cancer algorithm) every 4 months and annual transvaginal ultrasonography (55). Risk-reducing surgery was encouraged throughout the study. Cases of cancer that were detected during the UK-FOCSS screening trial were more often early stage compared with cases of cancer diagnosed more than 1 year after screening ended. A significant number of cases of cancer were identified at risk-reducing surgery. Survival analysis could not be performed. The authors concluded that screening may be an option for women at high risk of ovarian cancer who defer or decline risk-reducing salpingo-oophorectomy (55). Further investigation is necessary to identify better serum markers and improved screening algorithms to improve the positive and negative predictive value of testing.

Risk-Reducing Agents

A large systematic review and meta-analysis confirmed risk reduction with combined hormonal contraceptive use specifically in *BRCA* carriers. The reported reduction with 1 year of use was estimated at 33–80% for *BRCA1* and 58–63% for *BRCA2* carriers (56). Given the magnitude of the potential benefits (eg, ovarian and endometrial cancer risk reduction, pregnancy

prevention, cycle regulation), it is appropriate for women with mutations in *BRCA1* or *BRCA2* to use oral contraceptives if indicated, and use for cancer prophylaxis is reasonable. Although there have been conflicting reports in the literature on the effect of oral contraceptives on breast cancer risk (17), a recent meta-analysis showed no clear increased risk of breast cancer in *BRCA* mutation carriers who used oral contraceptives (57, 58).

Surgical Risk Reduction

Risk-Reducing Bilateral Salpingo-oophorectomy

The most effective ovarian cancer risk-reduction strategy for women with known *BRCA* mutations remains risk-reducing bilateral salpingo-oophorectomy (removal of the ovaries and fallopian tubes in their entirety). Women with *BRCA* mutations or who carry another actionable deleterious mutation predisposing to ovarian cancer should be offered risk-reducing bilateral salpingo-oophorectomy. The current National Comprehensive Cancer Network guidelines recommend that bilateral salpingo-oophorectomy also be considered for carriers of *BRIP1*, *RAD51C*, and *RAD51D* at ages 45–50 years and that hysterectomy along with bilateral salpingo-oophorectomy be considered for those with Lynch syndrome (17).

Meta-analysis results show that risk-reducing bilateral salpingo-oophorectomy reduces the risk of ovarian cancer, fallopian tube cancer, or peritoneal cancer by approximately 80% (hazard ratio, 0.21; 95% CI, 0.12–0.39) in women with known mutations in *BRCA1* or *BRCA2* (59). In addition, risk-reducing bilateral salpingo-oophorectomy has been shown to decrease overall mortality in women with a *BRCA1* or *BRCA2* mutation (60–62). Reported adverse effects of risk-reducing bilateral salpingo-oophorectomy include symptoms of early menopause (eg, vasomotor symptoms and decreased sexual functioning) and surgery complications (eg, wound infection, bladder perforation, small bowel obstruction, and uterine perforation) (49).

The timing of risk-reducing bilateral salpingo-oophorectomy can be individualized based on the particular genetic mutation, the patient's desires for further childbearing, and family history. Typically, risk-reducing salpingo-oophorectomy is recommended at age 35–40 years for *BRCA1* carriers with the highest lifetime risk of ovarian cancer, whereas women with *BRCA2* may consider delaying until age 40–45 years because of later onset of ovarian cancer (17). Ovarian cancer will be diagnosed in less than 2–3% of women with *BRCA1* or *BRCA2* mutations before age 40 years. For women

with *BRCA1* mutations, the risk of ovarian cancer markedly increases during their 40s, with 10–21% of *BRCA1* mutation carriers developing ovarian cancer by age 50 years. The risk of premenopausal ovarian cancer is much lower in *BRCA2* mutation carriers, with no more than 3% of *BRCA2* mutation carriers developing ovarian cancer by age 50 years (20, 63). Given the different timing of ovarian cancer risk, consideration can be given to counseling patients with *BRCA1* mutations differently than patients with *BRCA2* mutations. However, women with *BRCA2* mutations have a 26–34% chance of developing breast cancer by age 50 years (13, 18, 20), and the maximum benefit of removing the ovaries for breast cancer risk reduction is achieved the earlier the ovaries are removed (64, 65). Given these issues, the timing of risk-reducing salpingo-oophorectomy should be based on individual patient needs, taking into consideration the woman's desire to preserve fertility or prevent premature surgical menopause with the age-dependent effect of risk-reducing salpingo-oophorectomy on breast cancer and gynecologic cancer risks.

Bilateral Salpingectomy

Bilateral salpingectomy alone in high-risk women is not currently recommended for ovarian cancer risk reduction, although clinical trials are underway (17). There is increasing interest in risk-reducing bilateral salpingectomy as an option for women with *BRCA* mutations. This option is primarily driven by the desire of high-risk women to reduce the risk of ovarian cancer but also to avoid the adverse effects of early menopause that occur with removal of the ovaries. However, bilateral salpingectomy with oophorectomy may have the added benefit of reducing breast cancer risk, which is an important consideration given that many of these high-risk women are often also at increased risk of breast cancer. Population data for women at average risk confirm a marked ovarian cancer risk reduction of up to 65% for those receiving a bilateral salpingectomy (66, 67), but trials are still ongoing for high-risk women. One study created a theoretical model to quantify the potential risk of a staged bilateral salpingectomy followed by a delayed oophorectomy and estimated that the differences in ovarian cancer risk were very small (68). Thus, in high-risk women who are undergoing tubal sterilization for contraception, bilateral salpingectomy followed by future oophorectomy may be a reasonable option to offer (69). Women at high risk of ovarian cancer should be counseled that the efficacy of bilateral salpingectomy intended solely for ovarian cancer risk reduction remains under evaluation and that bilateral salpingectomy without oophorectomy does not provide added protection against breast cancer.

► ***How should women with mutations in BRCA1 or BRCA2 be counseled to reduce the risk of breast cancer?***

Current strategies to reduce the risk of breast cancer in women with known deleterious *BRCA* mutations include increased surveillance with more intensive breast cancer screening, chemoprevention, and surgery.

Screening

For women aged 25–29 years with known *BRCA* mutations, recommended breast cancer surveillance includes clinical breast examination every 6–12 months and annual radiographic screening (preferably, magnetic resonance imaging [MRI] with contrast) (17). Magnetic resonance imaging of the breast with contrast is preferred over annual mammography from ages 25–29 years because of evidence of radiation exposure leading to an increased breast cancer risk in European women with *BRCA* mutations who were exposed to mammography before age 30 years (70), even though this finding was not replicated in a North American cohort (71). For women aged 30 years and older with known *BRCA* mutations or other actionable breast cancer mutations, recommended breast cancer surveillance includes annual mammography and annual breast MRI with contrast, often alternating every 6 months (17). Magnetic resonance imaging is more sensitive for the detection of breast cancer than mammography, and the combination of MRI, mammography, and clinical breast examination has the highest sensitivity for the detection of breast cancer in high-risk *BRCA* mutation carriers (72–74).

Potential adverse effects of intensive breast cancer screening in women with increased familial risk (including *BRCA* mutation carriers) include false-positive test results, unnecessary imaging, unneeded surgeries, discomfort, pain, and anxiety (49). Systematic review evidence shows that compared with mammography, MRI is associated with higher rates of false-positive test results (8.2–14% MRI; 4.6–15% mammography), recall (11% MRI; 3.9% mammography), and unneeded biopsy (25–43% MRI; 27–28% mammography) (49). Reported rates of discomfort, pain, and anxiety do not differ significantly between MRI, mammography, and clinical breast examination (49).

Risk-Reducing Agents

The risk-reduction agents tamoxifen and raloxifene (in postmenopausal women) may be considered for breast cancer risk-reduction in *BRCA* mutation carriers. Studies have suggested that chemoprevention with tamoxifen may reduce breast cancer risk by approximately 62%

in *BRCA2* mutation carriers (75). This is similar to the reduction observed in estrogen-positive breast cancer after tamoxifen use among the general population (76). In contrast, tamoxifen has not been found to reduce the risk of breast cancer among *BRCA1* mutation carriers (75). This likely reflects the lower prevalence (10–24%) of estrogen receptor-positive breast cancer among *BRCA1* mutation carriers; whereas *BRCA2* mutation carriers have tumors that are predominantly (65–79%) estrogen receptor positive (75).

In a systematic review and meta-analysis of published studies of breast cancer risk-reducing medications, raloxifene was found to reduce invasive breast cancer in women at increased risk, including those with a family history of breast cancer, although none of the trials evaluated breast cancer incidence specifically in women who were *BRCA* mutation carriers (77). There was a decreased risk of invasive breast cancer over 5 years in women who received raloxifene (relative risk [RR], 0.44; 95% CI, 0.27–0.71) compared with women randomized to placebo. In the only head-to-head trial in the analysis, tamoxifen was associated with a greater risk reduction than raloxifene (RR of invasive cancer for raloxifene, 1.24; 95% CI, 1.05–1.47). Both medications were associated with a decreased risk of estrogen receptor-positive breast cancer but not estrogen receptor-negative breast cancer (77).

Commonly reported adverse effects of tamoxifen include vasomotor symptoms and vaginal symptoms (discharge, itching, dryness, and dyspareunia) (77). Tamoxifen also is associated with an increased risk of thromboembolic events (RR, 1.93; 95% CI, 1.41–2.64) and endometrial cancer (RR, 2.13; 95% CI, 1.36–3.32) (77). Reported adverse effects of raloxifene include vasomotor symptoms, leg cramps, dyspareunia, and weight gain (77).

Two trials have shown a reduction in breast cancer in postmenopausal high-risk women who use aromatase inhibitors. Neither trial specifically studied women with *BRCA* mutations. Given the protective effects in other at-risk populations, aromatase inhibitors may be an alternative for women who cannot take tamoxifen (78, 79).

Risk-Reducing Surgery

Bilateral Mastectomy

Women with *BRCA* mutations or who carry another actionable deleterious mutation that is predisposing to breast cancer should be offered risk-reducing bilateral mastectomy. Bilateral mastectomy reduces the risk of breast cancer in *BRCA* mutation carriers by 85–100% depending on the type of mastectomy procedure (49, 80, 81). The National Comprehensive Cancer Network

and U.S. Preventive Services Task Force recommend discussion of this option with the patient (17, 43). Total mastectomy removes the entire breast tissue, nipple, and areola, whereas a nipple-sparing mastectomy removes all breast tissue except the nipple and areola. There have been no trials that compared the efficacy of the two methods. Consideration of a contralateral prophylactic mastectomy is strongly recommended for *BRCA*-mutation carriers with breast cancer, given the 30% risk of contralateral recurrence in the 10 years following initial diagnosis (82).

Complete discussion with the patient who is considering prophylactic mastectomy is important and should include the psychosocial effects of mastectomy as well as the short-term and long-term complications (83). A meta-analysis of four descriptive studies of the effects of risk-reducing mastectomy with or without breast reconstruction found that adverse physical events included a 3–59 % risk of surgical complications (eg, postoperative infection, hematoma, flap necrosis, and failed reconstruction) and a 64–87% risk of postsurgical physical symptoms (eg, pain, numbness, tingling, swelling, and breast hardness) (49). In a retrospective cohort study of the psychosocial effects of risk-reducing bilateral mastectomy after a mean follow-up of 14.5 years, 70% of the 572 participants reported being satisfied with their decision to undergo surgery, and 74% reported decreased anxiety and concern about breast cancer (84). Commonly reported adverse psychosocial effects include decreased sexual satisfaction and negative body image (49, 85).

Bilateral Salpingo-Oophorectomy

Risk-reducing bilateral salpingo-oophorectomy for ovarian cancer prevention may have the added benefit of reducing the risk of breast cancer by 37–100% in *BRCA* mutation carriers (49). In addition, risk-reducing bilateral salpingo-oophorectomy may improve breast cancer outcomes and prevent subsequent ovarian cancer in *BRCA*-positive women with breast cancer (86, 87). The protective effect against breast cancer likely occurs only if patients are premenopausal at the time of risk-reducing bilateral salpingo-oophorectomy (87). In a large 2016 prospective study, premenopausal oophorectomy was associated with prevention of premenopausal breast cancer (before age 50 years) in *BRCA2* mutation carriers (age-adjusted hazard ratio, 0.18; 95% CI, 0.05–0.63) but not in *BRCA1* mutation carriers (age-adjusted hazard ratio, 0.79; 95% CI, 0.55–1.13) (88).

However, some researchers have called into question the breast cancer risk reduction from bilateral salpingo-oophorectomy. In one study, by using different analytics and adjusting for cancer at the time of test

and time preceding risk-reducing bilateral salpingo-oophorectomy, the authors found no decrease in breast cancer risk associated with risk-reducing bilateral salpingo-oophorectomy (89).

► *How should risk-reducing salpingo-oophorectomy be technically performed? How should surgical specimens be examined?*

For a risk-reducing bilateral salpingo-oophorectomy, all tissue from the ovaries and fallopian tubes should be removed. Thorough visualization of the peritoneal surfaces with pelvic washings should be performed. Complete, serial sectioning of the ovaries and fallopian tubes is necessary, with microscopic examination for occult cancer. The optimal approach will depend on patient and physician preference and the availability of an experienced health care provider to perform adequate staging. Decisions about the surgical approach should be made as part of an informed decision-making process, combining the patient's values and preferences with the knowledge and capability of the surgeon.

The diaphragm, liver, omentum, bowel, paracolic gutters, and appendix should be inspected in the abdomen. The ovaries, fallopian tubes, uterus, bladder serosa, and cul-de-sac should be inspected in the pelvis. Any abnormal areas should undergo biopsy. The ovarian vessels should be isolated and ligated approximately 2 cm proximal to the end of identifiable ovarian tissue to ensure that all ovarian and tubal tissue is completely removed. If a hysterectomy is not being performed, the fallopian tube should be divided at its insertion into the uterine cornu and the ovary removed at the utero-ovarian ligament as close to the uterus as possible. When performing a laparoscopic procedure, to optimize preservation of the ovarian surface epithelium, the specimens can be placed in an endoscopic bag before removal from the abdomen. If gross unsuspected cancer is identified, surgical staging with lymphadenectomy and omentectomy may be performed at the time of risk-reducing surgery, provided appropriate preoperative consent has been obtained. It also is reasonable, however, to await final pathology test results and proceed with definitive surgery in an expeditious manner if cancer is identified. Routine performance of an intraoperative frozen section procedure is discouraged because most malignancies found at risk-reducing salpingo-oophorectomy are occult (90).

Complete, serial sectioning of the ovaries and fallopian tubes is necessary, with microscopic examination for occult cancer (91). Occult, microscopic cancer of the ovary or fallopian tube has been identified in *BRCA1*

and *BRCA2* mutation carriers undergoing prophylactic risk-reducing salpingo-oophorectomy (92–95). This is more common in women older than 45 years than in younger women.

Thorough pathology review of the ovaries and the fallopian tubes is critical in order to detect microscopic cancer in these high-risk women. Rather than taking only one or two representative sections from each ovary, the complete ovaries and fallopian tubes should be serially sectioned and evaluated (91). In fact, more cases of microscopic fallopian tube cancer have been detected than microscopic ovarian cancer in the prophylactic risk-reducing salpingo-oophorectomy specimens of *BRCA1* and *BRCA2* mutation carriers. Although the tumors identified are microscopic, they are often high grade, and information from the peritoneal lavage may reflect the aggressiveness of the disease (96). Because occult cancer may be found only through serial sectioning and thorough evaluation of the ovaries and tubes, it is possible that some subsequent primary peritoneal carcinoma actually represents the recurrence of a previously unrecognized occult cancer (97).

The decision to perform a concurrent hysterectomy should be individualized. Salpingo-oophorectomy alone confers a significant cancer risk reduction with less surgical risk and shorter postoperative recovery (98, 99). However, benefits of hysterectomy include a more simplified hormone therapy strategy (with estrogen only) and the removal of the cornual fallopian tube, which is associated with a theoretical increased risk of cancer (100). The potentially increased risk of high-grade histology endometrial cancer in *BRCA1* mutations carriers also can be discussed and patient preferences taken into account (38). In addition, hysterectomy may be considered when there are other medical indications for removal of the uterus and cervix. For women taking tamoxifen, hysterectomy may be considered to reduce their endometrial cancer risk (101, 102).

► ***What follow-up should women with mutations in *BRCA1* or *BRCA2* receive after risk-reducing salpingo-oophorectomy?***

Women with mutations in *BRCA1* or *BRCA2* who undergo risk-reducing salpingo-oophorectomy by the recommended age of 35–45 years will experience early menopause and the possibility of associated symptoms, and may have long-term health outcomes of heart disease and bone loss. Women who have undergone risk-reducing salpingo-oophorectomy and who are unaffected by breast cancer should be offered hormone therapy to mitigate the effects of early menopause. Patients should be counseled that limited data suggest that use

of estrogen-only or combination hormone therapy for a few years does not significantly diminish the protective effect of risk-reducing bilateral salpingo-oophorectomy on breast cancer risk reduction (103). However, the effect of long-term hormone therapy on breast cancer risk reduction in the patient who is premenopausal at time of risk-reducing salpingo-oophorectomy is not known. There are only two small studies that have looked at the safety of hormone therapy in this cohort after risk-reducing salpingo-oophorectomy (104, 105).

► ***What surveillance for primary peritoneal cancer should be performed for women after risk-reducing salpingo-oophorectomy?***

No laboratory or imaging surveillance is recommended for primary peritoneal cancer in women who have undergone risk-reducing salpingo-oophorectomy. The benefit of serum CA 125 measurement or imaging surveillance after risk-reducing salpingo-oophorectomy is not known because peritoneal cancer is relatively uncommon (1–6% cumulative risk for all carriers) (105). Patients should be informed that because screening for primary peritoneal cancer is investigational, there is limited information available regarding the relative risks and benefits. Counseling should include information about symptom awareness and a discussion of the need to continue routine well-women screenings and care.

► ***How should women with *BRCA* mutations be counseled regarding fertility and quality of life?***

There have been contradictory reports on whether women with *BRCA* mutations, particularly *BRCA1* mutations, without a history of cancer and who have not undergone risk-reducing surgery have an increased incidence of premature menopause (106–108). Recent evidence suggests that *BRCA1* mutation carriers may have decreased ovarian reserve (as measured by circulating anti-müllerian hormone levels) compared with *BRCA2* carriers and noncarriers (109). Nevertheless, fertility often is affected because many women with *BRCA* mutations will have breast cancer at a young age and undergo chemotherapy. The recommendation for offering a risk-reducing salpingo-oophorectomy by age 35–45 years also limits the fertility window. This warrants a careful discussion with a young *BRCA* carrier to ensure that her fertility needs are met. Those facing a cancer diagnosis or a decision for risk-reducing surgery may be candidates for oocyte or embryo cryopreservation (110).

Menopausal symptoms, including hot flashes, sexual discomfort (resulting from vaginal atrophy), and reduced libido are common in women who have

undergone risk-reducing salpingo-oophorectomy. For women without a history of breast cancer, hormone therapy can mitigate many of these symptoms. Quality-of-life studies of high-risk women who have undergone risk-reducing salpingo-oophorectomy demonstrate no significant change in their quality of life, except for a subset who report decreased sexual satisfaction (49). *BRCA* mutation carriers may benefit from supportive services, including counseling for sexuality and adjustment (111, 112).

► ***What is the appropriate management for a woman with a strong family history who does not have a documented mutation in *BRCA1*, *BRCA2*, or other hereditary breast and ovarian cancer-associated gene?***

Women who have a personal or family history of breast or ovarian cancer but who do not have a documented mutation in *BRCA1*, *BRCA2*, or other hereditary breast or ovarian cancer-associated gene should be managed based on their family history. Preliminary data have suggested that women from families with a history of only breast cancer (but not ovarian cancer) in which no *BRCA* mutation is identified remain at a significantly increased risk of breast cancer, but not ovarian cancer (113, 114). Most cases of inherited predisposition to ovarian cancer are caused by pathogenic variants in *BRCA1*, *BRCA2*, or the other hereditary breast and ovarian cancer-associated genes (Table 1), although there may be other less prevalent genes that have not yet been identified (115). If women were tested before 2009, they may not have had large gene rearrangement testing in the *BRCA* genes (ie, the *BRCA* Rearrangement Test). Furthermore, women tested before 2013 would not have had access to multigene panel testing. For these women, further consultation with a specialist in cancer genetics may help to clarify their residual risk and the need for additional testing. It is important for high-risk individuals to stay in contact with clinicians experienced in the care of women at increased risk of hereditary breast and ovarian cancer, given the continued and rapidly developing research and refinements in testing technology.

Summary of Recommendations

The following recommendations are based on good and consistent scientific evidence (Level B):

- Genetic counseling is recommended for all women with ovarian epithelial cancer (this includes fallo-

pian tube cancer or primary peritoneal cancer) and for individuals who have a personal or family history of breast cancer or ovarian cancer.

- Women with *BRCA* mutations or who carry another actionable deleterious mutation that is predisposing to breast cancer should be offered risk-reducing bilateral mastectomy.
- Women with *BRCA* mutations or who carry another actionable deleterious mutation predisposing to ovarian cancer should be offered risk-reducing bilateral salpingo-oophorectomy. The timing of risk-reducing bilateral salpingo-oophorectomy can be individualized based on the particular genetic mutation, the patient's desires for future childbearing, and family history. Typically, risk-reducing salpingo-oophorectomy is recommended at age 35–40 years for *BRCA1* carriers with the highest lifetime risk of ovarian cancer, whereas women with *BRCA2* may consider delaying until age 40–45 years because of later onset of ovarian cancer.
- For a risk-reducing bilateral salpingo-oophorectomy, all tissue from the ovaries and fallopian tubes should be removed. Thorough visualization of the peritoneal surfaces with pelvic washings should be performed. Complete, serial sectioning of the ovaries and fallopian tubes is necessary, with microscopic examination for occult cancer.

The following recommendations are based primarily on consensus and expert opinion (Level C):

- Evaluating a patient's risk of hereditary breast and ovarian cancer syndrome should be a routine part of obstetric and gynecologic practice. Initial risk evaluation should include a personal medical history and family history.
- Genetic testing is recommended when the results of a detailed risk assessment that is performed as part of genetic counseling suggest the presence of an inherited cancer syndrome for which specific genes have been identified and when the results of testing are likely to influence medical management.
- The two main genetic testing options for hereditary breast and ovarian cancer syndrome are *BRCA* mutation testing and multigene panel testing that includes both *BRCA* and other genetic mutations. Multigene panel testing may be useful when more than one gene may be associated with an inherited cancer syndrome or when a patient has a personal or family history that is consistent with an inherited cancer susceptibility, but single-gene testing has not identified a pathogenic variant.

- ▶ In women with *BRCA* mutations or who have a personal or family history of ovarian cancer, routine ovarian cancer screening with measurement of serum CA 125 level or transvaginal ultrasonography generally is not recommended. Transvaginal ultrasonography or measurement of serum CA 125 level may be reasonable for short-term surveillance in women at high risk of ovarian cancer starting at age 30–35 years until the time they choose to pursue risk-reducing bilateral salpingo-oophorectomy, which is the only proven intervention to reduce ovarian cancer-specific mortality.
- ▶ For women aged 25–29 years with known *BRCA* mutations, recommended breast cancer surveillance includes clinical breast examination every 6–12 months and annual radiographic screening (preferably, MRI with contrast).
- ▶ For women aged 30 years and older with known *BRCA* mutations or other actionable breast cancer mutations, recommended breast cancer surveillance includes annual mammography and annual breast MRI with contrast, often alternating every 6 months.
- ▶ Women who have a personal or family history of breast or ovarian cancer but who do not have a documented mutation in *BRCA1*, *BRCA2*, or other hereditary breast or ovarian cancer-associated gene should be managed based on their family history.

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ISSN 1099-3630

The American College of Obstetricians and Gynecologists
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Hereditary breast and ovarian cancer syndrome. Practice Bulletin No. 182. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2017;130:e110–26.

The MEDLINE database, the Cochrane Library, and ACOG's own internal resources and documents were used to conduct a literature search to locate relevant articles published between January 2000 and May 2017. The search was restricted to articles published in the English language. Priority was given to articles reporting results of original research, although review articles and commentaries also were consulted. Abstracts of research presented at symposia and scientific conferences were not considered adequate for inclusion in this document. Guidelines published by organizations or institutions such as the National Institutes of Health and the American College of Obstetricians and Gynecologists were reviewed, and additional studies were located by reviewing bibliographies of identified articles. When reliable research was not available, expert opinions from obstetrician–gynecologists were used.

Studies were reviewed and evaluated for quality according to the method outlined by the U.S. Preventive Services Task Force:

- I Evidence obtained from at least one properly designed randomized controlled trial.
- II-1 Evidence obtained from well-designed controlled trials without randomization.
- II-2 Evidence obtained from well-designed cohort or case–control analytic studies, preferably from more than one center or research group.
- II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments also could be regarded as this type of evidence.
- III Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

Based on the highest level of evidence found in the data, recommendations are provided and graded according to the following categories:

Level A—Recommendations are based on good and consistent scientific evidence.

Level B—Recommendations are based on limited or inconsistent scientific evidence.

Level C—Recommendations are based primarily on consensus and expert opinion.

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Exhibit 3

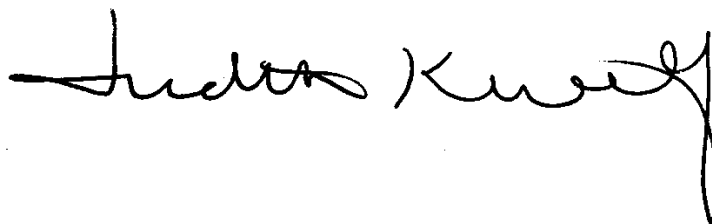
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MDL NO. 16-2738 (FLW) (LHG)

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**RULE 26 EXPERT REPORT OF
JUDITH WOLF, MD**

A handwritten signature in black ink, appearing to read "Judith Wolf", with a long, sweeping vertical line extending downwards from the end of the signature.

Date: November 16, 2018

Judith Wolf, MD

I. BIOGRAPHY AND QUALIFICATIONS

I am a board certified gynecologic oncologist, a physician specializing in the care of women with cancer with more than thirty years experience. I attended medical school at Northeast Ohio Universities College of Medicine and then moved to Texas where I completed residency at the University of Texas San Antonio and fellowship at MD Anderson Cancer Center where I remained on faculty for more than twenty years as Professor in the Department of Gynecologic Oncology. My area of expertise is ovarian cancer - diagnosis, research, treatment, and patient advocacy.

I have authored or co-authored over 100 peer-reviewed research articles and was the principal investigator or co-investigator for eleven research grants related to gynecologic cancers. Additionally, I have served as the principal investigator, co-principal investigator, or collaborator on 84 protocols, and have presented at more than 50 conferences, as well as at numerous scientific exhibitions and seminars. The majority of these have dealt with some aspect of ovarian cancer.

My research began when I was a fellow in gynecologic oncology. In addition to two years of clinical training, I spent two years working in the lab and getting my Masters degree in Biomedical Science from The University of Texas School of Biomedical Sciences in Houston. My research as a graduate student was in investigating targets for therapy in ovarian cancer. One of these led to a phase I Clinical trial for women with ovarian cancer using a targeted therapy. This trial was part of a larger NCI grant. After completing training, I maintained a research lab for over ten years, investigating gene therapy for the treatment of both ovarian and cervical cancer. My laboratory research in ovarian cancer led to a Clinical trial of gene therapy for women with ovarian cancer. Being able to see the long road it takes to bring new therapies from the lab to clinic fostered my continued interest in clinical trials, and led me to become involved in both investigator initiated and NCI cooperative group clinical trials - Phase II and III trials of new therapies for ovarian cancer.

Throughout my tenure as a Professor at MD Anderson Cancer Center, I was recruited to join the biomedical industry. It wasn't until in 2014, when Vermillion at Diagnostic Company recruited me as a Chief Medical Officer that I felt compelled to make a change in my career path. By this point in time, I had cared for hundreds of women with ovarian cancer, and saw the devastation this disease causes, with little improvement in the overall prognosis in more than twenty years. Working with a diagnostic company, focused on the early detection of ovarian cancer, seemed to me to be another way I could work to make a difference. While at Vermillion, I co-authored several publications, helped the company gain FDA clearance for their second generation multiprotein biomarker assay for ovarian cancer detection and was integral in the company obtaining a \$7.5 million dollar grant from the State of Texas for ovarian cancer detection.

After two years at Vermillion, I was recruited by another small start-up diagnostic company, ProvistaDx, again in a Chief Medical Officer role. ProvistaDx was using similar multi-protein assays (like Vermillion) but combining them with antibodies to try to detect both breast and

ovarian cancer early. While at ProvistaDx, we published several articles in the breast cancer detection area and their first publication using this combined technology for ovarian cancer detection.

Working in these diagnostic companies exposed me to some of the intricacies of working in the biomedical industry and research from a view- from that as a public ally traded company (Vemillion) and a small private start-up (ProvistaDx). Additionally, I learned much about the regulation of the industry.

In mid-2018 I left my company position to have more time to focus on my volunteer and advocacy work for women's health- with a large focus on ovarian cancer.

In the mid 1990s, I became involved with raising awareness and educating women about ovarian cancer through my work with the National Ovarian Cancer Coalition. Initially, I was a medical board member and am currently a governing board member. Our mission is to raise awareness and educate women and their families about ovarian cancer. Additionally, I combined my love of running and passion for ovarian cancer to organize a charity 5K walk/run to raise awareness and research money for the Blanton/ Davis Ovarian Cancer Research Program at MD Anderson Cancer Center. This race has been going on now for more than twenty years and has raised more than \$5 million dollars for ovarian cancer research.

In 2014, I became a member of the board of the Society for Women's Health Research which is a National nonprofit dedicated to promoting research on biological differences in disease and improving women's health. Additionally, I began working with Health Volunteers Overseas. I have volunteered in Vietnam, Honduras and Haiti working with physicians in these countries to train them to be better able to care for women with gynecologic cancers. Working with HVO, for the past year and a half, I am heading a project training young surgeons in Nepal to care for women with ovarian, cervical and uterine cancers. To continue my mission of improving women's health here in the US, I am working part time in Indianapolis, IN as a Gynecologic Oncologist. My curriculum vitae is attached as Exhibit A.

II. METHODOLOGY

I was asked to make a determination as to whether the genital use of talcum powder can cause ovarian cancer. I approached this issue in a similar way and with the same rigor that I would use in my professional practice, both clinically and in research. This is an exercise I have used regularly throughout my thirty plus year career. I reviewed extensive medical and scientific literature (including epidemiological, animal, mechanistic studies, and reviews on all relevant topics). I also researched publicly available information related to talcum powder products, their safety, and their association with ovarian cancer. Many of these sources were obtained through articles and references from my personal library of journals, textbooks, as well as PubMed searches on relevant topics. Additional relevant literature, documents, and testimony were provided by the attorneys working on this case. I also requested additional information on various relevant issues when appropriate.

In doing this research, I applied the same standards that I use in clinical medicine to consider the reliability and validity of the medical and scientific literature, assessing the evidence according to the strengths and weaknesses of the study under review. I considered an extensive body of relevant literature, without regard to the nature of the specific findings. I based the opinions provided in this report using a weight of the evidence methodology in the context of Bradford Hill concepts.

III. OVERVIEW OF OVARIAN CANCER

Ovarian cancer is a group of malignancies that are believed to begin in ovarian or fallopian tube tissue. There are three groups of cancers based on the cell type from which they arise - germ cell, stromal, and epithelial cancers. Epithelial cancers (EOC) account for the vast majority of ovarian cancers (greater than 90%) and are further subdivided based on the microscopic characteristics of the cells. These subtypes include serous, endometrioid, clear cell, mucinous, undifferentiated or mixed. Of these, serous is by far the most common and accounts for 70% of EOC. Epithelial ovarian cancers are those that are associated with talcum powder products.

Epithelial carcinoma of the ovary, fallopian tube, and peritoneum are usually considered as a single entity due to their common clinical behavior, risk factors, and pathogenesis. Over the past decade, research has found that many serous carcinomas of the ovary may begin in the cells that line the distal portion of the fallopian tube. These cells then leak, drip, or “escape” from the tube and the ovary (which is next to the tube) or the peritoneum (the layer that lines the inside of the abdomen and pelvis). (Levanon 2008, Chen et al. 2017; Singh et al. 2016; Soong et al. 2018) Cancers that clinically appear to arise from the fallopian tube, ovary or peritoneum have the same microscopic appearance, pattern of spread (throughout the pelvis and abdomen), and response to treatment. This information is consistent with the role of talcum powder in cancer development.

Ovarian cancer is a relatively rare cancer. The American Cancer Society estimates in 2018 22,240 new cases of ovarian cancer compared to 268,670 new cases of breast cancer.¹ There is no screening for ovarian cancer and symptoms are vague. This presentation leads to late diagnosis for more than 75% of patients. Because of these factors and the often aggressive nature of the tumors, ovarian cancer is the most deadly gynecologic malignancy in the U.S. Seventy to seventy-five percent of women with advanced stage EOC die from their disease, usually from bowel obstruction, following years of chemotherapy treatment.² (Chen, L-M, et al 2018).

The National Cancer Institute defines a risk factor as something that increases the chances of developing a disease. Associations can occur that are not actually linked with a disease. A causative risk factor is one that increases the chances of developing a disease by means of a

¹ <https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2018/cancer-facts-and-figures-2018.pdf>

² *Id.*

known or predictable mechanism. In other words, it is more than a mere association. (Vineis 2017).

The most significant risk factor associated with ovarian cancer are inherited susceptibility genes, primarily BRCA1, BRCA2, and the mismatch repair genes (associated with Lynch syndrome). A woman with BRCA1 gene mutation has a 39-46% lifetime risk of developing ovarian cancer; a woman with BRCA2 gene mutation has an 11-27% lifetime risk of developing ovarian cancer. (Ring et al. 2017). It is estimated that these hereditary gene mutations account for 10-15% of all ovarian cancer and 75% of all hereditary ovarian cancers. (Lancaster et al. 2015). It is important to distinguish these inherited gene mutations from induced mutations caused by inflammation or environmental insults.

In addition to talc and asbestos exposure, other risk factors that have been linked to EOC include increasing age, nulliparity, infertility, endometriosis, obesity, polycystic ovarian syndrome, use of an intrauterine device, history of pelvic inflammatory disease, and cigarette smoking (for mucinous carcinoma). Protective factors (associated with a decreased risk of EOC) include previous pregnancy, history of breastfeeding, oral contraceptives, and tubal ligation. (Hunn and Rodriguez 2012; Mallen, Townsend, and Tworoger 2018; Park et al. 2018; Folkins et al. 2018). It is important to note that risk factors can interact with each other or act independently. They can act in a cumulative, additive, and/or synergistic fashion. (Wu et al. 2018; Vitonis et al. 2011).

Talcum powder dusting is often referred to as a “lifestyle factor”. There are no medical benefits; any risk, particularly a risk of something as devastating and deadly as ovarian cancer, is unacceptable. (Folkins et al. 2018) Because of this, I advise all my patients not to use talcum powder products or to stop using them if they are already doing so.

Most women with EOC present with pelvic or abdominal pain, bloating, and/or gastrointestinal symptoms. Diagnosis is based upon pathologic evaluation of tissue. Knowledge and evaluation of the pathology of ovarian cancer is part of every gynecologic oncologist’s training and experience. Staging is surgical. In a patient with advanced stage ovarian cancer (stage 3 and 4), the cancer is spread throughout the abdomen and pelvis with typically thousands of tumor nodules covering the surface of all internal organs, along with several liters of fluid containing cancer cells (ascites).

Treatment for ovarian cancer is a combination of surgery and chemotherapy. Most women with advanced disease obtain 1-2 years of remission after treatment, and then their cancer recurs. Once ovarian cancer recurs, it is not curable and most patients spend the remainder of their life on chemotherapy in an attempt to extend their life spans and minimize their often severe symptoms.

IV. HISTORICAL BACKGROUND OF TALC

Johnson and Johnson’s baby powder was introduced to consumers in 1894. (Gurowitz 2007).

In the late 1940s and early 1950s, there were numerous articles (including at least one from Johnson and Johnson's own lab) describing the inflammatory properties of talc when introduced into the peritoneal cavity experimentally or through surgical gloves and the relative safety of starch products in the same setting. (Eberl and George 1948; Graham and Jenkins 1952). In 1953, Johnson and Johnson submitted a patent application for a "non-irritating" starch-based dusting powder due to the severe postoperative complications and strong inflammatory reaction frequently caused by talc. (Caldwell et al. 1953). In 1967, the association between asbestos and ovarian cancer was reported (J. Graham and Graham 1967).

Henderson first identified talc particles deep in ovarian tissue in 1971. (Henderson et al. 1971). Dr. Woodruff and colleagues at Johns Hopkins began raising awareness regarding environmental toxins like talc as etiologic factors in the pathogenesis of ovarian cancer in the early 1970s. (Parmley and Woodruff 1974).

In 1979, Longo and Young cautioned the cosmetic industry regarding the dangers of talc in *The Lancet*: "Epidemiological, experimental, and clinical data seem to link asbestos and talc with ovarian cancer. Direct passage of talc or asbestos-contaminated talc through the female reproductive tract to the ovarian surface may play an aetiological role. Further systematic evaluation of talc and asbestos as ovarian carcinogens is needed. . . . What is disturbing is that a consultant to the cosmetic industry feels that further research on the biological effects of talc 'merits little priority'". (D. L. Longo and Young 1979). The first epidemiologic study on the association between talc and ovarian cancer was published in 1982. (Cramer et al. 1982).

Between 1992 and 1995, concerns were raised in the medical literature regarding risks, including ovarian cancer, of talc on condoms. (e.g., Kang, Griffin, and Ellis 1992; Kasper and Chandler 1995). In 1995, the condom industry voluntarily agreed to stop dusting condoms with talc due to ovarian cancer concerns. ("PCPC_MDL00062175" 1999; McCullough 1996). Recommendations regarding the use of talcum powder on diaphragms were also discontinued in the late 1990s. In 1998, Janssen, a subsidiary of Johnson & Johnson, changed the warning on its All-Flex Diaphragm to state "Powders should not be used with the diaphragm."³

V. EPIDEMIOLOGY

Since the early 1980's, there have been numerous epidemiological studies evaluating the risk of ovarian cancer with talcum powder usage. To the present time, there are over 25 case-control studies, three prospective cohort studies, one pooled analysis, and seven meta-analyses. I assessed all of these studies.

A case-control study is designed to help determine if an exposure is associated with an outcome, in this case ovarian cancer. First, researchers identify women with and without ovarian cancer - cases and controls. Then they look back in time to learn which subjects in each group had talcum

³ Janssen sold the Ortho diaphragms beginning in the 1960s. The 1962 instructions stated, "Dust diaphragm when dry with talcum powder and return it to the original container." (JANSSEN-000001-19) 1962).

powder exposure(s), comparing the frequency of the exposure in the case group to the control group.

A case-control study is always retrospective because it starts with an outcome then traces it back to investigate exposures. Advantages of case-control studies are that they are comparatively efficient, less expensive, and easier to perform. Potential weaknesses include selection bias, (because they are not randomized) and recall bias. Case-control studies are particularly appropriate for uncommon diseases, like ovarian cancer, in which a very large cohort would be required to accumulate enough cases for analysis. (Narod 2016).

A cohort study follows a group of people with defined characteristics, such as talcum powder exposure, and who are followed to determine incidence of an outcome, in this case development of ovarian cancer. Cohort studies can be retrospective or prospective. They can calculate rates of disease in exposed and unexposed individuals for multiple outcomes over time. Potential disadvantages of cohort studies include the requirement of large number of subjects for rare exposures and outcomes and long duration of follow up for certain conditions.⁴ These disadvantages apply to the study of talc and ovarian cancer. Narod estimated that, for a cohort study to be properly powered to accurately predict the risk associated with talc use and ovarian cancer, as many as 200,000 women may be necessary. (Narod 2016).

A meta-analysis combines the results from previous studies to derive conclusions from a larger set of data. Outcomes from a meta-analysis may include a more precise estimate of the effect of treatment or exposure (talcum powder) than any individual study contributing to the pooled analysis.⁵ A meta-analysis weights the strengths of the studies before combining the data, unlike a pooled study. A meta-analysis can be especially useful to review a complex, sometimes conflicting body of literature.

A randomized control trial, in which participants are divided by chance into separate groups to compare different interventions, is considered the gold standard in some research situations. However, it would be unethical and impractical to conduct a prospective randomized control clinical trial to compare the outcomes of women who did and did not use genital talcum powder because of its known carcinogenic potential.

For this project, I reviewed all epidemiological studies related to talcum powder and ovarian cancer, but concentrated on the cohort studies, the meta-analyses, and more recent high-quality case-control studies. I critically analyzed factors such as study design, journal quality, number of subjects, length of follow-up, and potential biases.

Case-Control Studies

There are numerous case-control studies. Overall, the case-control studies are consistent showing a 30-50% increase in risk of ovarian cancer with talcum powder use. I found the most

⁴ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2998589/>

⁵ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3049418/>

recent ones to be the most useful, based on their size and quality of design. Several are summarized below:

A study by Wu published in 2015, evaluated 1701 women with EOC in California. The conclusion of this study found that talc significantly increased the risk of ovarian cancer – 40% in whites, 20% in Hispanics, and 56% (not statistically significant) in African Americans. The number of African Americans with ovarian cancer was only 128 and may account for the non-significant increase. (Wu et al. 2015).

Cramer published a recent case-control study of nearly 4,000 women in Massachusetts and New Hampshire with ovarian cancer and found that genital use of talcum powder, either alone or in combination with body use, was associated with a statistically significant elevated epithelial ovarian cancer risk (OR 1.33). Risk increased with frequency and duration of use. Talcum powder use increased risk for serous and endometrioid tumors with the dose response most apparent for invasive serous cancer. (Cramer et al. 2016).

A multi-center study sponsored by National Cancer Institute of epithelial ovarian cancer in African-American women, a group with a high prevalence of talcum powder use, determined that regular genital powder use was associated with an increased risk of epithelial ovarian cancer (OR 1.44). A dose-response relationship was found for duration of use and number of lifetime applications ($P < 0.05$). Additionally, talcum powder use was common (62.8% of cases and 52.9% of controls). (Schildkraut et al. 2016).

Cohort Studies

The Nurses' Health Study (NHS) is a prospective study of 121,700 nurses who were aged 30-55 years at enrollment in 1976 and followed through 1996 at the time of the publication. In the NHS, talcum powder use was ascertained once in 1982, the same year as the first case-control study showing an association of talc use with ovarian cancer. (Cramer et al. 1982). The follow up period for this study was 12.9 years. The study concluded there was no overall association with talc "ever use" and epithelial ovarian cancer. However, there was a statistically significant increase risk of invasive serous ovarian cancer (40%) that was higher with more frequent talcum powder use. The short period of follow up may not account for all ovarian cancer cases due to latency considerations between talcum powder usage and the development of ovarian cancer. (Gertig et al. 2000). A second report of the Nurses' Health Study in 2010 did not find a statistically significant increased risk with talcum powder usage and either epithelial cancer as a whole or serous subtype. (Gates et al. 2010).

The Women's Health Initiative (WHI) enrolled 93,676 women from 1993-1998. Women were eligible if they were aged 50 to 79 (mean 63.3 years) at enrollment and postmenopausal. Mean follow-up was 12.2 years. Use of powder on the genitals was associated with 12% increased risk of ovarian cancer, though this was not statistically significant. Limitations of this study include lack of information regarding oophorectomy and recall bias regarding history of talc "ever use". Additionally, the short follow-up may not account for all cases of ovarian cancer. Information regarding the frequency or duration of powder usage was not obtained. (Houghton et al. 2014).

The Sister Study (2003-2009) followed 50,884 women in the US and Puerto Rico who had a sister diagnosed with breast cancer. At enrollment, participants were asked about douching and talcum powder use in the previous twelve months. During follow-up (median 6.6 years) 154 women reported a diagnosis of ovarian cancer but only seventeen of those reported talc use. The authors determined that there was little association between baseline talcum powder use and subsequent ovarian cancer. Douching at baseline, more common in talc users, was associated with increased risk. All ovarian cancers were grouped together. Limitations of this study include: 1) talc use was only obtained at baseline and was uncommon (analysis was based on only 17 cases), 2) no histologic information was obtained, so it is impossible to analyze relationship to serous subtype, 3) no risk elevation has ever been reported with dusting of diaphragm, cervical cap, or sanitary napkins, and 4) the short follow-up fails to account for the latency period. (Gonzalez et al. 2016).

All of the cohort studies are limited by lack of power, failure to make the appropriate queries, selection bias, and short follow-up.

Meta-Analyses

A recent and comprehensive meta-analysis by Penninkilampi and Eslick, published in 2018, included 24 case-control (13,421 cases) and three cohort studies (890 cases). The authors found that “any” perineal talc use was associated with an increased risk of ovarian cancer (OR = 1.31; 95% CI = 1.24, 1.39). More than 3600 lifetime applications (OR = 1.42; 95% CI 1.25, 1.39) were slightly more associated with ovarian cancer than <3600 (OR = 1.32; 95% CI = 1.15, 1.50). An association with “ever use” of talc was found in case-control studies (OR = 1.35; 95% CI = 1.27, 1.42), but not cohort studies (OR 1.06; 95% CI = 0.90, 1.25). However, cohort studies did find an association between talc use and invasive serous ovarian cancer (OR = 1.25; 95% CI = 1.01, 1.55).

The authors stated that case-control studies are preferred in this situation because statistical power is easier to obtain with the larger number of ovarian cancer cases and controls and the lengthy follow-up necessary for a prospective study is not required. I agree. The authors determined that perineal talc use is associated with a 24%–39% increased risk of ovarian cancer that is suggestive of a causal association. (Penninkilampi and Eslick 2017).

Summary of Epidemiological Evidence

When looking at epidemiological studies in their totality, the data demonstrates a consistent, replicated, and statistically significant increased risk of developing epithelial ovarian cancer with perineal talcum powder use. Invasive serous carcinoma is the most commonly associated histologic subtype. The risk elevation is 20-60%. This risk is stable among case-control studies, one cohort study, and all meta-analyses/pooled analyses over several decades. Recall and confounding bias in case-control studies appear to have minimal impact. (Penninkilampi and Eslick 2018; Langseth et al. 2008). There appears to be no significant publication bias. (Berge et al. 2017; Penninkilampi and Eslick 2018). Meta-analysis is the most reliable and scientifically valid epidemiological methodology in this setting - the evaluation of the association of talcum powder usage with ovarian cancer risk

VI. ASBESTOS AND OTHER CONSTITUENTS OF TALCUM POWDER

Asbestos is one of the most potent carcinogens known. All forms of asbestos (chrysotile, crocidolite, amosite, tremolite, actinolite, and anthophyllite) are carcinogenic to humans. (IARC 2012) The conclusions reached by International Agency for Research on Cancer (IARC) about asbestos and its carcinogenic risks apply to these six types of asbestos wherever they are found, and *includes talc containing asbestiform fibres* (fibrous talc). (IARC 2012). Asbestos was first linked to pulmonary mesothelioma in 1935 (Gloyne 1935) and has been known to be an etiologic factor for ovarian cancer since 1965. (J. Graham and Graham 1967).

According to IARC, asbestos causes mesothelioma of the lung, larynx, *and ovary*. Based on multiple positive cohort mortality studies of women with heavy occupational exposure to asbestos, IARC's Working Group determined there is a causal association between asbestos exposure and ovarian cancer. (IARC 2012).

The scientific literature, Johnson and Johnson testing results and documents, and testing results of Dr. William Longo and Dr. Mark Rigler have demonstrated that talcum powder products, including Johnson's Baby Powder and Shower to Shower, may contain asbestos. (Cralley et al. 1968; Rohl et al. 1976; Lockey 1981; Paoletti et al. 1984; Blount 1991; Werner 1982; "Deposition of Alice M. Blount, Ph.D., Circuit Court of the City of St. Louis State of Missouri, Case No.: 1522-CC10417-01" 2018; Exhibit 28, Deposition of John Hopkins, Ph.D., MDL No. 2378, 2018; Exhibit 47, Deposition of Julie Pier, MDL 2738, 2018).

The IARC 2012 Monograph on asbestos states, "consumer products (e.g., cosmetics, pharmaceuticals) are the primary source of exposure to talc for the general population. Inhalation and *dermal contact* (i.e., through perineal application of talcum powders) are the primary routes of exposure."(IARC 2012).

Asbestos exposure is known to cause ovarian cancer; its presence in Johnson and Johnson talcum powder products contributes to the carcinogenicity of the products through an established mechanism of inflammation, DNA damage, and genetic alterations. Asbestos fibers may directly induce DNA damage mediated by reactive oxygen species. Asbestos fibers have also been shown to physically interfere with the mitotic apparatus, which may result in aneuploidy or polyploidy, and specific chromosomal alterations characteristic of asbestos-related cancer. In addition, persistent inflammation and macrophage activation can secondarily generate additional reactive oxygen species and reactive nitrogen species that can indirectly induce genotoxicity in addition to activation of intracellular signaling pathways, resistance to apoptosis, stimulation of cell proliferation, induction of epigenetic alterations, and activation of oncogenes/inactivation of tumor suppressor genes. (IARC 2012; Kane et al. 1996; Mossman 2018; Shukla et al. 2009; M. C. Jaurand 1997, 1989; M. Jaurand 1991)

In addition to asbestos, talcum powder products have been shown to contain fibrous talc, nickel, and chromium. These are Group 1 carcinogens according to IARC. The inflammatory mechanism for carcinogenesis described by IARC is similar to that described for asbestos and talcum powder. These products also contain cobalt which is a Group 2b carcinogen according to

IARC (possibly carcinogenic), defined previously in this report.(W. E. Longo and Rigler 2018; Exhibit 47, Deposition of Julie Pier, MDL 2738, 2018)

I have also seen the list of “fragrance chemicals” added to Johnson’s Baby Powder and Shower to Shower products, as well as the expert report of Dr. Michael Crowley. Many of these chemicals are known to be irritants, toxins, and carcinogens. Some have been shown to be harmful to the reproductive organs and function. These chemicals would be expected to accompany the talcum powder as it migrates or is transported through the genital tract to the fallopian tubes and ovaries. At least some of these chemicals would also be expected to be absorbed through the vaginal mucosa. These chemicals likely contribute to the inflammatory properties, toxicity, and carcinogenicity of these talcum powder products.

The presence of these constituents provides support for the mechanism for the increased risk seen in the epidemiological studies.

VII. MIGRATION AND TRANSPORT OF TALC THROUGH THE GENITAL TRACT

In the adult female, the peritoneal cavity communicates with the outside via the fallopian tubes, uterus, and vagina. It is universally accepted in the gynecologic community that substances migrate and/or be transported in both directions. Evidence to support this includes, but is not limited to:

1. Sperm: Sperm move more quickly through the genital tract than would be predicted from innate motility, indicating a transport mechanism. In addition, dead sperm and inanimate sperm particles (lacking flagella) are efficiently transported upwards through the uterus and tubes. (Jones and Lopez 2006). This process involves directed uterine contractility that has been confirmed through research of intrauterine pressure measurements. (Kissler et al. 2004).
2. Carbon particles: Inert carbon particles were placed in the posterior vaginal fornix and observed in the fallopian tubes 28 and 34 minutes later (2 out of 3 patients tested). This research confirmed that sperm motility is not the chief factor in transport and that contractions of the uterus are likely involved in process of migration/transport of particles through the genital tract. (Egli and Newton 1961).
3. Retrograde menstruation: The transport of menstrual flow into the peritoneal cavity was first proposed by Sampson in 1927 and is now well-established as the mechanism for endometriosis initiation. The prevalence of retrograde menstruation has been described in 90% of investigated women. (Blumenkrantz et al. 1981; Halme et al. 1984).
4. Particulate radioactive material: Particulate radioactive material was placed in the posterior vaginal fornix. Twenty four hours later, radioactive material was present in the adnexa separate from the uterus in 2/3 of cases. The authors concluded that the transit of particles from the vagina to the peritoneal cavity and the ovaries “is probably the same

for many chemical substances used for hygienic, cosmetic, or medicinal purposes, many of which may have potential carcinogenic or irritating properties . . . migration of certain chemical substances could play an important aetiological role in gynaecological diseases and especially in carcinoma of the ovary.” (Venter and Iturralde 1979).

5. “Uterine peristaltic pump”: Rapid and sustained sperm transport from the cervix to the fallopian tube is provided by uterine peristaltic contractions that can be visualized by vaginal sonography. (Kunz 1997; Zervomanoklakis et al. 2007).
6. Glove powder: Studies have demonstrated retrograde migration of starch after gynecological examination with powdered gloves. The authors concluded that: “Consequently, powder or any other potentially harmful substances that can migrate from the vagina should be avoided.” (Sjösten, Ellis, and Edelstam 2004).
7. Talc: Studies have documented the presence of talc particles in the adnexa, ovaries, and peritoneum. The authors of these studies have concluded that this occurs as a result of migration of talc particles from the vagina through the cervix, uterus, and fallopian tubes. (Henderson et al. 1971; D. W. Cramer 1999; Heller et al. 1996). Talc has also been noted in pelvic lymph nodes which could also occur through migration, absorption, or inhalation with transport through the lymphatic system. (Cramer et al. 2007).

The migration of particles, including talc, asbestos and other constituents of talcum powder products, from the vagina to the upper genital tract (tubes and ovaries) is a key element in the mechanism by which talcum powder products cause ovarian cancer. The evidence supporting this process is robust and universally accepted by the medical community.⁶ (FDA Citizens Petition response) I have considered the limited evidence to the contrary and find it non-persuasive.

In addition to perineal application resulting in migration and transport of particles through the genital tract, inhalation of these particles is another recognized route of exposure. (IARC 2012; W. E. Longo, Rigler, and Egeland 2017; Steiling et al. 2018; Daniel W. Cramer et al. 2007) With either of these routes, talcum powder components can also be directly absorbed into the lymphatic system and bloodstream.

VIII. INFLAMMATION AND MOLECULAR BASIS FOR CARCINOGENESIS OF TALCUM POWDER PRODUCTS

The link between inflammation and cancer has been recognized since the 1800s. Inflammation and oxidative stress increase the risk of cancer, including ovarian cancer. It has been known since the 1940’s that talc increases inflammation. (Balkwill and Mantovani 2001; Eberl and George 1948).

⁶ FDA states that the “potential for particulates to migrate from the perineum and vagina to the peritoneal cavity is indisputable.

There is an increased risk of malignancy with many inflammatory processes, including infection, autoimmune diseases, hypoxia, and chemical and physical agents (including talc and asbestos).

1. Virchow noted inflammatory cells (leukocytes) in neoplastic tissue as early as 1863.
2. Both tumor cells and inflammatory cells produce cytokines and chemokines which can contribute to cancer growth and spread.
3. Cytokines from inflammation/oxidative stress can influence multiple steps of the neoplastic process: survival, growth, mutation, proliferation, differentiation, and movement of cells. (Balkwill and Mantovani 2001; Reuter et al. 2010; Crusz and Balkwill 2015; Kiraly et al. 2015). Below are examples of inflammatory cytokines and their influence on cancer:
 - a. Tumor necrosing factor (TNF) can induce reactive oxygen (nitric oxygen (NO)) which can cause DNA damage. DNA damage can also occur by inhibiting cytochrome p450.
 - b. Migration inhibitory factor (MIF) can inhibit the activity of p53 which is a tumor suppressor.
 - c. IL-6, IL-1, IL-8 are all known to stimulate tumor cell proliferation and survival.
 - d. Multiple inflammatory cytokines (TNF, IL-1, IL-6, TGF beta 1) can stimulate angiogenesis.
 - e. TNF and IL-1 stimulate adhesion to promote invasion and metastasis of cancer cells.
4. Inflammation/oxidative stress affects all phases of cancer development and growth and is implicated in pathogenesis of ovarian cancer. This leads to decreased apoptosis and increased anaerobic metabolism. Anaerobic metabolism leads to an acidic state which facilitates cancer growth. (G. Saed 2017; G. M. Saed et al. 2010; Jiang et al. 2011; Shan and Liu 2009; Freedman et al. 2004)
5. Talcum powder causes inflammation/oxidative stress both *in vitro* and *in vivo* (in both animal and human tissues). (Eberl and George 1948; Graham and Jenkins 1952; Hamilton et al. 1984; Buz'Zard and Lau 2007; Shukla et al. 2009; G. Saed 2017; G. M. Saed et al. 2010; G. Saed 2017; Fletcher, Nicole, Memaj, Ira, and Saed, Ghassan 2018; N. Fletcher and Saed 2018, 2018; N. M. Fletcher et al. 2017, 2011; "NTP Toxicology and Carcinogenesis Studies of Talc (CAS No. 14807-96-6)(NonAsbestiform) in F344/N.Rats and B6C3Fl Mice (Inhalation Studies)" 1993; Keskin et al. 2009).
6. In a recently reported abstract, Harper and Saed describes induction gene point mutations after talcum powder exposure, corresponding to known specific single nucleotide polymorphisms (SNPs) in normal and ovarian cancer cells. These SNPs alter the activities of key oxidant enzymes and enhance the pro-oxidant state. (Harper and Saed 2019). This process of gene mutation is part of the carcinogenic cascade initiated by inflammation.
7. Although the literature is still somewhat contradictory, aspirin and other non-steroidal anti-inflammatory drugs have been shown to prevent and treat certain types of cancer, particularly colorectal.(Trabert et al. 2019; Rayburn, Ezell, and Zhang 2009; Chan et al. 2005).

Inflammation/oxidative stress has been well established as a significant factor in the development of cancer, including ovarian cancer. Inflammation/oxidative stress facilitates cancer growth at multiple steps. Inflammation/oxidative stress is an early step in the molecular pathway by which talc causes ovarian cancer.⁷

IX. CORNSTARCH

Since 1948 with a publication from Johnson & Johnson's, own laboratory, it has been clear that starch is a safer alternative to talc for use on surgical gloves. Starch, unlike talc, is not an irritant and can be absorbed readily. (Eberl and George 1948).

A review paper by Whysner and Mohan in 2000 evaluated the available literature regarding the effects of cornstarch in the peritoneal cavity, comparing the potential risk of ovarian cancer with cornstarch versus talc. Unlike talc, the authors noted that 1) cornstarch is capable of being removed by physiologic processes from the peritoneal cavity, 2) cornstarch contains no asbestos, and 3) epidemiologic studies reviewed found no relationship between cornstarch powder use and ovarian cancer. The authors concluded that any increased risk for ovarian cancer as a result of perineal exposure to cornstarch was biologically implausible. (Whysner and Mohan 2000).

X. DETERMINING WHETHER A RISK FACTOR IS CAUSATIVE

Although Bradford Hill factors are primarily an epidemiologic tool, the general principles provide a framework for clinical doctors to assess whether diseases like cancer can be caused by a particular agent, condition, or practice. These considerations are the same as those that I apply regularly, both in my clinical practice and research.

The factors as described by Bradford Hill are:

1. Strength (effect size): A small association does not mean that there is not a causal effect, though the larger the association, the more likely that it is causal.
2. Consistency (reproducibility): Consistent findings observed by different persons in different places with different samples strengthens the likelihood of an effect.
3. Specificity: Causation is more likely if there is a specific disease with no other likely explanation. Most frequently used example is a specific bacterium causing a particular disease (e.g. *M. tuberculosis* causes TB and *T. pallidum* causes syphilis). The more specific an association between a factor and an effect is, the bigger the probability of a causal relationship, but this is not necessarily required.

⁷ Richard Zazenski, Director Product Safety for Luzenac, states in an email to Bill Ashton, on September 30, 2004: "I came across this paper this morning published in the April, 2004 journal "Human Reproduction", an official journal of the European Society for Human Reproduction and Embryology. It offers some compelling evidence **in support of the** 'migration' hypothesis. Combine this 'evidence' with the theory that talc deposition on the ovarian epithelium initiates epithelium inflammation – which leads to epithelium carcinogenesis – and you have a potential formula for NTP classifying talc as a causative agent in ovarian cancer." (IMERY5137677-IMERY5137690).

4. Temporality (and Latency): The effect must occur after the cause (and if there is an expectant delay between the cause and expected effect, then the effect must occur after that delay).
5. Biological gradient (Dose-response): Greater exposure should generally lead to greater incidence of the effect. There may also be a minimum level of exposure necessary (threshold). As a general principle of pharmacology and toxicology, the likelihood of a response increases with longer and more frequent exposure to an agent (dosage). (Klaassen and Doull 2013).
6. Plausibility: A plausible mechanism between cause and effect is helpful (but Hill noted that knowledge of the mechanism can be limited by current knowledge). Knowledge and an understanding of the biological mechanisms changes over time.
7. Coherence: Coherence between epidemiological and other research data/findings increases the likelihood of an effect. Coherence is the idea that an alleged association should not conflict with substantive knowledge that exists regarding the disease at issue.
8. Experiment: "Occasionally it is possible to appeal to experimental evidence". This factor often refers to support from animal and clinical research with sound methodology. Has there been an attempt to collect data to analyze a cause and effect relationship? Do studies use controls when feasible? Are experiments reproducible? Are there ethical limitations?
9. Analogy: The effect of similar factors may be considered. All the rules relating to scientific methodology must be employed at each stage of the analogy. (Fedak et al. 2015).

I considered these aspects of a causal relationship in determining whether talcum powder products cause ovarian cancer.

Strength

Overall the studies show a 1.3-1.4 odds ratio of increased risk of ovarian cancer among perineal talc users. The most recent and most complete meta-analysis determined an odds ratio of 1.31 with any perineal talc use and the development of ovarian cancer. An association with ever use of talc was found in case-control studies (OR = 1.35), but not cohort studies (OR = 1.06). However, cohort studies found an association between talc use and invasive serous type ovarian cancer (OR = 1.25). (Penninkilampi and Eslick 2018).

If invasive serous ovarian cancer is considered exclusively, the association is even stronger.

In general, many of the studies are well conducted, numerous and consistent, making the strength of the association valid. When looking at causation of a relatively rare disease like ovarian cancer, this magnitude of risk is statistically and clinically significant and not unusual. With ovarian cancer, a disease which is difficult to diagnose and deadly, any preventable risk factor (talcum powder) should be deemed critically important and avoided.

Consistency

The magnitude of risk has been consistent over three decades, across various geographic populations and throughout the United States, Canada, and Australia. Results are generally consistent across case-control, meta-analysis, and pooled analysis studies. (Penninkilampi and Eslick 2018). I deemed the consistency and replication of the studies to be important in my causation analysis.

Specificity

The most compelling disease associated with talcum powder use is epithelial ovarian cancer, therefore specificity for a disease is demonstrated.

Temporality

Exposure to talcum powder and the resultant development of ovarian cancer meets the temporality consideration that the outcome follows the event. The average latency period between exposure to talc and diagnosis of ovarian cancer is at least twenty years. This is consistent with other cancers known to be caused by chemicals and/or toxins. (Purdie et al. 2003; Okada 2007)

Biologic Gradient (Dose-response)

Exposure is difficult to quantify with talcum powder applications with regard to how much is used, where it is concentrated, and how much actually reaches the tubes and ovaries; Many of the studies did not obtain the necessary information to evaluate dose response and lacked adequate power to assess dose-response accurately. Despite the lack of sufficient information in many studies, recent meta-analyses/pooled study and a case-control studies do show a dose response, using frequency and duration of use as parameters. (Penninkilampi and Eslick 2018; Cramer et al. 2016; Schildkraut et al. 2016; Terry et al. 2013; A. H. Wu et al. 2015). Modern medicine also recognizes that a monotonic dose-response curve is often overly simplistic (e.g. asbestos demonstrates a threshold rather a linear dose-response). Response can vary based on unique characteristics of the given population, exposure routes, molecular endpoints, individual susceptibility and synergistic or antagonistic effects of cumulative exposures. (Fedak et al. 2015). Given the limitations of the data, I consider this a less important factor when compared to the strength of the association, consistency, and the biological mechanism.

Plausibility

The general mechanism by which talcum powder products cause ovarian cancer is established as an inflammation-induced process. It is well-accepted that particles reach the fallopian tubes and ovaries through migration/transport through the genital tract. These particles can also reach the pelvic organs through inhalation. The particles elicit an inflammatory tissue response and initiate a cascade of events and pathways at the cellular level that result in cancer formation. This process is well-described by the medical and scientific community. In addition, as previously discussed in this report, various components of talcum powder products, including asbestos and fibrous talc, are known carcinogens and known to cause cancer by similar mechanisms.

Coherence

The findings and conclusions from epidemiological, animal, and in vitro studies are coherent with what is known about ovarian cancer. There is also consistency with what is known about other gynecological malignancies and other cancers induced by environmental and occupational exposures.

Experiment

Causation of ovarian cancer by talcum powder is supported by laboratory (*in vitro* and *in vivo*) experiments. Research is ongoing which will further elucidate specific processes.

Prospective randomized controlled clinical trials to evaluate talcum powder products and their relationship to ovarian cancer are not feasible for a variety of ethical and methodological reasons. These include the recognized toxicity of talc, asbestos, and other constituents of talcum powder, the absence of therapeutic benefit, the long latency period, and the seriousness of ovarian cancer.

Analogy

As with consistency, plausibility, and coherence, the association between talcum powder and ovarian cancer is analogous to other diseases caused by various and specific carcinogens. For example, smoking causes lung cancer, asbestos causes mesothelioma and ovarian cancer, sun exposure causes skin cancer, and HPV causes cervical cancer. All of these cancers are the result of an inflammatory process initiated by a foreign agent.

XI. SUMMARY OF OPINIONS

The opinions in this report are provided to a reasonable degree of medical and scientific certainty. A summary of these opinions follows:

1. Based on epidemiological studies, the established biological mechanism, and evidence of the presence of asbestos and other known carcinogens, talcum powder products cause epithelial ovarian cancer in some women. The genital use of talcum powder products presents a significant risk factor for ovarian cancer for *all* women who use the products.
2. When looking at epidemiological studies in their totality, the data demonstrates a consistent, replicated, and statistically significant increased risk of developing epithelial ovarian cancer with perineal talcum powder use.
3. Asbestos is one of the most potent human carcinogens and known to cause ovarian cancer. The presence of asbestos in talcum powder products contributes to their carcinogenicity. In addition, other known constituents of talcum powder products (including nickel, chromium, and cobalt) are carcinogenic and their presence likely contributes to the cancer-causing properties of talcum powder products.

4. The extensive number of fragrance chemicals added to the talcum powder products likely contributes to the inflammatory properties, toxicity, and carcinogenicity of these products.
5. The migration/transport of particles, including talc and asbestos, to the upper genital tract (tubes and ovaries) is a key element in the mechanism by which talcum powder products cause ovarian cancer. The evidence supporting migration is robust and universally accepted by the gynecologic community. In addition to perineal application resulting in migration and transport of particles through the genital tract, inhalation of these particles is another recognized route of exposure.
6. Inflammation/oxidative stress is an early and essential step in the molecular process by which talcum powder products cause ovarian cancer.
7. Cornstarch is a safer alternative to talcum powder.
8. Talcum powder use is a preventable causative risk factor for EOC.

Based on my education, training, experience and expertise in ovarian and other gynecologic cancers, review of the totality of the evidence, analysis and weighing the data in the context of Bradford Hill, it is my professional opinion that talcum powder products cause epithelial ovarian cancer in some women. The use of talcum powder products presents a significant risk factor for ovarian cancer in *all* women who use the products.

I reserve the right to amend or modify the report as new information becomes available.

I have not testified in litigation over the previous 4 years. I am charging \$600 per hour for my work on this matter.

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Exhibit A

CURRICULUM VITAE

Judith K Wolf, MD

PRESENT TITLE AND AFFILIATION

**Chief Medical Officer
ProvistaDx
55 Broad St 18th Floor
New York, NY 0004**

CITIZENSHIP

United States

OFFICE ADDRESS

**ProvistaDx
55 Broad St 18th Floor
New York, NY 0004**

PREVIOUS WORK EXPERIENCE

Chief Medical Officer

Vermillion, Inc

12117 Bee Caves Rd

Austin TX 78738

9/2014-6/2016

Division Chief of Surgery

Banner MD Anderson Cancer Center

**2946 E Banner Gateway Dr
Gilbert, AZ 85235**

6/2011-9/2014

Faculty

The University of Texas MD Anderson Cancer Center

1515 Holcombe Blvd

Houston, TX 77030

7/1995-6/2011

EDUCATION

Degree-Granting Education

University of Akron, Akron, OH, BS, 1982, Natural Sciences

Northeastern Ohio Universities College of Medicine, Rootstown, OH, MD, 1986, Biomedical Science

The University of Texas Health Science Center at Houston, Houston, TX, MS, 1993, Biomedical Sciences- Thesis, Characterization of two populations of the human ovarian cancer cell line, 2774, that express different levels of epidermal growth factor receptor.

Postgraduate Training

Residency, Obstetrics and Gynecology

U.T. Health Science Center at San Antonio, San Antonio, TX, Dr. Carl J. Pauerstein

1986-1990

Fellowship, Gynecologic Surgery

University of Minnesota, Duluth, MN, Dr. Leo Twiggs

1990-1991

Fellow, Gynecologic Oncology, Department of Biology

The University of Texas MD Anderson Cancer Center, Houston, TX, Dr. J Taylor Wharton 1991-1993

Junior Faculty Associate, Gynecologic Oncology The University of Texas MD Anderson Cancer Center, Houston, TX, Dr. J. Taylor Wharton 1993-1995

CREDENTIALS

Board Certification

American Board of Obstetrics and Gynecology, (Written Exam), 1990

American Board of Obstetrics and Gynecology: Special Qualification in Gynecologic Oncology, (Written Exam), 1996

American Board of Obstetrics and Gynecology, 1997

-Recertified 2014

American Board of Obstetrics and Gynecology: Special Qualification in Gynecologic Oncology, 2000

-Recertified 2014

Licensures

Active

State of Arizona, AZ, 45110, 7/2011 – current

State of Indiana, IN 01074549B, 9/2014- current

State of Georgia, GA 173182 6/2014- present

Inactive

State of Minnesota, MN, 1/1990–1/1993

State of Texas, TX, H4856, 1988–8/2012

EXPERIENCE/SERVICE

Academic Appointments

Assistant Professor, Department of Gynecologic Oncology, Division of Surgery, The University of Texas M.D. Anderson Cancer Center, Houston, TX, 1995–1999

Assistant Professor, Department of Gynecologic Oncology, Division of Surgery, The University of Texas M.D. Anderson Cancer Center, Houston, TX, 1999–2002

Associate Professor, Department of Gynecologic Oncology, Division of Surgery, The University of Texas M.D. Anderson Cancer Center, Houston, TX, 2002–8/2008

Graduate Faculty, Biomedical Sciences, Graduate School of Biomedical Sciences, The University of Texas Houston Health Science Center, Houston, TX, 2003–2011

Associate Professor, Department of Gynecologic Oncology, Blanton Davis Ovarian Cancer Research Program, The University of Texas M. D. Anderson Cancer Center, Houston, TX, 2006–8/2008

Associate Director, Department of Gynecologic Oncology, Developmental Therapeutics,

The University of Texas MD Anderson Cancer Center, Houston, TX, 2006–2011

Co-Division Director, Department of Gynecologic Oncology, Division of Surgery, Baylor College of Medicine, Houston, TX, 4/2006–4/2007

Professor, Department of Gynecologic Oncology, Blanton Davis Ovarian Cancer Research Program, The University of Texas MD Anderson Cancer Center, Houston, TX, 2008–2011

Associate Director, Department of Gynecologic Oncology, Developmental Therapeutics, The University of Texas MD Anderson Cancer Center, Houston, TX, 2011

Division Chief, Surgical Oncology, Banner MD Anderson Cancer Center, Gilbert, AZ 6/2011–9/2014

Vice Chair, Department of Oncology Services, Banner MD Anderson Cancer Center, Gilbert, AZ 6/2011–9/2014

Adjunct Professor, Gynecologic Oncology, University of Texas, MD Anderson Cancer Center, Houston, Texas, 2012–2014

Clinical Professor, Division of Clinical Education, Arizona College of Osteopathic Medicine, Midwestern University, Arizona, 2012–2014

Administrative Appointments/Responsibilities

Assistant Program Director (Research), Fellowship in Gynecologic Oncology, Division of Surgery, The University of Texas M. D. Anderson Cancer Center, Houston, TX, 1999–2004

Medical Director, Community Relations, Department of Gynecologic Oncology, Division of Surgery, The University of Texas MD Anderson Cancer Center, Houston, TX, 4/2008–2011

Other Appointments/Responsibilities

Member, Felix Rutledge Society, Houston, TX, 1995–Present

President, Felix Rutledge Society, 2008–2009

Member, Society of Gynecologic Oncologists, Chicago, IL, 1996–Present

Member, Quality and Outcomes Committee, Society of Gynecologic Oncology, 2012–Present

Member, Breakthrough Series: Improving Care at the End of Life, Houston, TX, 1997–2011

Founder-Chairman, Sprint for Life 5K Fun Run, M. D. Anderson Cancer Center, Houston, TX, 1998–Present
Chairman, Medical and Scientific Advisory Board, National Ovarian Cancer Coalition, Dallas, TX, 2003–Present
President, Houston Gynecologic & Obstetrics Society, Houston, TX, 2003–2004
Treasurer, Houston Gynecologic & Obstetrics Society, Houston, TX, 1998–2000
Vice President, Houston Gynecologic & Obstetrics Society, Houston, TX, 2001–
Member, Gynecologic Oncology Group, Philadelphia, PA, 2001–2011
Departmental Liaison, M D Anderson Cancer Center Women Faculty Programs, Houston, TX, 2/2010–2011

Endowed Positions

N/A

Consultantships

N/A

Military or Other Governmental Service

N/A

Institutional Committee Activities

Medical Records Committee, Member, 1995–2011
Clinical Research Committee, Member, 1997–2000
Women's Faculty Administrative Organization Steering Committee, Member, 1998–1999
Cancer Committee, Hermann Hospital, Member, 1998–2001
Search Committee, Anesthesia, Member, 1999–2000
Ovarian SPORE Executive Committee, Member, 1999–2011
Student and Trainee Resources-Clinical Fellow's Research Award, Faculty Reviewer, 1999
Cancer Therapeutics Discovery Program Grants, Reviewer, 2000–2004
Clinical Research Committee, Member, 2001–2004
Search Committee, Internal Medicine, Member, 2001
Uterine SPORE Executive Committee, Member, 2003–2011
Faculty Promotion and Tenure Committee, Division of Surgery, Member, 2003–2011
Gynecologic Oncology Surgical Research Program (GO-SRP) Committee, Member, 2004–2011
Fellowship Planning Committee, Member, 2004–2011
Blanton-Davis Ovarian Cancer Research Program Executive Committee, Member, 2004–2011
Faculty Celebration Steering Committee, Member, 2004
Gynecologic Oncology Center for Surgical Research (GOCSR), Member, 2004
Ovarian Working Group, Department of Gynecologic Oncology, Chairman, 2005–2011
Search Committee, Department of Nephrology Chair, Member, 2005
Gynecologic Oncology T32 - Program Steering Committee, Member, 2005
The University of Texas M. D. Anderson Cancer Center, Gynecologic Oncology Group (GOG), Co-Principal Investigator, 2005–2011
Faculty Celebration Gala, Chairman, 2005
Faculty Leadership Committee, Member, 2006–2011
Executive Committee of Faculty Senate, Member, 2007–2009

Faculty Senate Committee, Chair Elect, 2010–2011
Faculty Senate Committee, Chair, 2011 – 2012
Faculty Senate Committee, Member, 2006–2011
Gynecologic Oncology Committee for New Institute of Personalized Cancer Therapy, Head, 4/2008–2011
Award Nomination Selection Committee, 2010–2011
Clinical Research Counsel, Member, 6/2008–2011
Clinical Research Committee, Member, 7/2009–2011
Women Faculty Programs, Member, 8/2009–2011
Charitable Activities Committee Subcommittee, Member, 2010–2011
OPPE/FPPE, Department Safety Officer, 2/2010–2011
Institutional Review Board 1 (IRB1), Associate Member, 8/2010–2011
Vice Chair, Department of Oncology Services, BMDACC, 2011- 2014

BMDACC Perioperative Logistic Committee, 2011- 2014

BMDACC Surgery Committee, 2011- 2014t

BMDACC Phase II Steering Committee, 2011-2014

Relationship Committee between UT MD Anderson Cancer Center and BMDACC, 2011- 2014

BMDACC Research Faculty Guidance Committee, 2011- 2014

Banner Medical Group Knowledge Management Committee, 2012- 2014

BMDACC, Affiliate of UTMDACC for Gynecologic Oncology Group (GOG), Principal Investigator, 2012-2014

BMDACC Biospecimen Governance Committee Chair 2013- 2014

BMDACC Research Committee, Co-chair 03/2013- 2014

Banner Health Oncology Steering Committee, 5-9/2014

HONORS AND AWARDS

Medical Honor Society, Alpha Omega Alpha, 1986

Galloway Fellowship in Gynecologic Oncology, Memorial Sloan Kettering Cancer Center, 1989

Best Doctors in America®, 2005–2006, 2006–2007, 2007–2008, 2011, 2013

RESEARCH

Grants and Contracts (past 5 years)

Funded

Principal Investigator-MDACC, J. S. Blanton Research Fund, J. S. Blanton Research Fund, 1999–2011, \$116,367

Principal Investigator, 10%, Gene Developmental in Ovarian Cancer, Specialized Program of Research Excellence, 2001– 2011, \$50,000

Principal Investigator, Gene Therapy Development Award, W. M. Keck Center for Cancer Gene Therapy Development Award, 2001– 2011, \$50,000

Principal Investigator, Texas Federation of Business Professional Women Award, Texas Federation of Business Professional Women Award, 2001– 2011, \$6,337

Principal Investigator, The Ovarian Cancer Survivors Fund, Don-Ray George & Associates, 2003 – 2011, \$116,126

Co-Investigator, Efficacy and Mechanism of SERMs for Recurrent / Advanced Endometrial Cancer, Molecular Progression of Endometrial Cancer, P150CA098258, Specialized Program of Research Excellence, PI - Karen H. Lu, 9/1/2003 – 8/31/2008, \$992,019

Principal Investigator-MDACC, Gynecologic Oncology Center for Surgical Research (GOCSR), Houston Jewish Community Foundation, 2004 – 2011, \$50,000

Principal Investigator-MDACC, Susan G. Koch Ovarian Cancer Research Fund, Susan G. Koch, 2005 – 2011, \$50,000

Co-Investigator, The University of Texas M D Anderson Cancer Center, Gynecologic Oncology Group, Gynecologic Oncology Group, PI - Robert Coleman, M.D., 2005 – 2011.

Pending

N/A

Other

N/A

Completed

Principal Investigator, Evaluation of the Effect and Mechanism of Action of Adenovirus-mediated Tumor Suppressor Gene Therapy of Ovarian Cancer, Gynecologic Cancer Foundation, 1998–2006, \$25,000

Co-Investigator, Evaluating Fatigue and Other Symptoms of Ovarian cancer Patients with Ecological Momentary Assessment, Ovarian Cancer Research Development Award, PI - Karen Basen Engquist, Ph.D., 1999–2006, \$50,000

Not Funded

N/A

Protocols

Funded

Principal Investigator, Evaluating Fatigue and Other Symptoms of Ovarian Cancer Patients with Ecological Momentary Assessment, ID99-, 1999, Ovarian Cancer Research Development Award

Principal Investigator, A Phase II Study of Oral Xeloda Administered Twice Daily for Fourteen Days Every Three Weeks to Patients with Advanced Ovarian, Tubal or Peritoneal Cancer Refractory to Platinum and Taxanes, GYN 00-275, 2000–2001

Co-Principal Investigator, Phase II Evaluation of Oxaliplatin In Persistent or Recurrent Squamous Cell Carcinoma of the Cervix, GOG127P, PI - Charles Levenback, 2000–2003, GOG

Principal Investigator, A Phase 1 Dose Escalation Study of Intraperitoneal E1A Lipid Complex (1:3) with Combination Chemotherapy in Women with Epithelial Ovarian Cancer, ID 99-316, 2000–2006

Co-Principal Investigator, A Phase II Evaluation of Thalidomide (NSC #66847, IND #48832) In the Treatment of recurrent or Persistent Leiomyosarcoma of the Uterus, GOG231B, PI - Diane Bodurka, 2001–2002, GOG

Co-Principal Investigator, A Phase II Multicenter Study of Oral Xeloda Administered Twice Daily for Fourteen Days Every Three Weeks to Patients with Advanced or Recurrent Cervical Cancer, GYN01-080, PI - Lois Ramondetta, M.D., 2001–2003

Collaborator, A 2-Part Phase I/II Study of Extended Field External Irradiation and Intracavitary Brachytherapy combined with Chemo (Weekly Cisplatin-Arm 1) and Amifostine (Weekly Cisplatin and Amifostine-Arm 2), RTOG-C0116, PI - Anuja Jhingran, M.D., 2001– 2011, RTOG

Principal Investigator, A Phase I/II Study to Evaluate the Maximum Biologic Dose of Pegylated-Interferon (PEG- INTRON) in Patients with Platinum Resistant Ovarian, Peritoneal, or Fallopian Tube Cancer, ID02-115, 2002–2005, \$100,000, Integrated Therapeutics Group/Schering Plough

Collaborator, A Phase II Evaluation of Decetaxel and Gemcitabine Plus G-CSF in the treatment of recurrent of Persistent Leiomyosarcoma of the Uterus, GOG-0131G, PI - Lois Ramondetta, M.D., 2002–2005, GOG

Collaborator, A Phase II Evaluation of Liposomal Doxorubicin (Doxil) in the Treatment of Persistent or

Recurrent Squamous Cell Carcinoma of the Cervix, GOG 127-R, PI - Diane Bodurka, M.D., 2002–2005, GOG

Co-Principal Investigator, Phase II Study of Irofulven (IND #48914) in Patients with Refractory or Recurrent Advanced Epithelial Ovarian Cancer Using Every-Other-Week Dosing, GYN01-486, PI - Diane Bodurka, 2002–2005

Collaborator, A Phase II Evaluation of Capecitabine (NSC#712807) in the Treatment of Persistent or Recurrent Non-squamous Cell Carcinoma of the Cervix, GOG-0128G, PI - Diane Bodurka, M.D., 2002–2011, GOG

Collaborator, Treatment of Patients with Stage IB2 Carcinoma of the Cervix: A Randomized Comparison of Radical Hysterectomy and Tailored Chemo-Radiation versus Chemo-radiation, GOG0201, PI - Charles Levenback, M.D., 2003–2005, GOG

Collaborator, A Randomized Study of Tamoxifen versus Thalidomide (NSC no.66847) in Patients with Biochemical-Recurrence- Only Epithelial Ovarian Cancer of the Fallopian Tube, and Primary Peritoneal Carcinoma after First-Line Chemotherapy, GOG-0198, PI - Robert Coleman, M.D., 2003–2006, GOG

Collaborator, A Phase I/II Study of COX-2 Inhibitor, Celebrex (Celecoxib), and Chemoradiation in Patients with Locally Advanced Cervical Cancer, RTOG-C0128, PI - Patricia Eifel, M.D., 2003–2011, RTOG

Principal Investigator, A Phase I/II Study of Gleevec/Taxol in Patients with Newly Diagnosed Stage IIIC or IV or Recurrent (any stage) Uterine Papillary Serous Carcinoma (UPSC), GYN03-0177, 2003–2011, Novartis

Collaborator, A Phase III Clinical Trial of Tisseel VH Fibrin Sealant to Reduce Lymphedema Incidence after Inguinal Lymph Node Dissection Performed in the Management of Vulvar Malignancies, GOG195, PI - Pedro Ramirez, M.D., 2003–2011, GOG

Collaborator, A Phase III Randomized Clinical Trial of Laparoscopic Pelvic & Para-Aortic Node Sampling with Vaginal Hysterectomy and BSO versus Open Laparotomy with Pelvic and Para-Aortic Node Sampling and Abdominal Hysterectomy and BSO in Endometrial Adenocarcinoma and Uterine Sarcoma, GOG-LAP2, PI - Pedro Ramirez, M.D., 2003–2011, GOG

Collaborator, A Phase III Randomized Trial of Paclitaxel and Carboplatin versus Triplet or Sequential Doublet Combinations in Patients with Epithelial Ovarian or Primary Peritoneal Cancer, GOG-0182, PI - John Kavanagh, M.D., 2003–2011, GOG

Collaborator, A Randomized Phase III Study of Paclitaxel plus Cisplatin versus Vinorelbine Plus Cisplatin versus Gemcitabine Plus Cisplatin versus Topotecan Plus Cisplatin in Stage IVB, Recurrent or Persistent Carcinoma of the Cervix, GOG-0204, PI - Charles Levenback, M.D., 2003–2011, GOG

Principal Investigator, Phase I/II Study of Weekly Topotecan and Iressa in Patients with Platinum-Resistant Ovarian/Peritoneal/Fallopian Tube Cancer, 2003-0322, 2004–2007, \$92,500, GlaxoSmithKline/Astra Zeneca

Principal Investigator, A Phase I/II Randomized Study of Intraperitoneal tDCC-E1A and Intravenous Paclitaxel in Women with Platinum-Resistant Ovarian Cancer, ID02-321, 2004–2011, \$365,000, Marcus Foundation Funds-UT M. D. Anderson Cancer Center

Principal Investigator, A Phase II Study of RAD001 in Patients with Recurrent Endometrial Cancer, 2004-0002 IND 69277, 2004–2011, \$111,300, Novartis

Collaborator, A Randomized, Phase II Trial of Doxorubicin/Cisplatin/Paclitaxel and G-CSF versus Carboplatin/Paclitaxel in Patients with Stage III and IV or Recurrent Endometrial Cancer, GOG-0209, PI - Lois Ramondetta, M.D., 2004–2011, GOG

Mentor, Training Grant - Department of Gynecologic Oncology, Training of Academic Gynecologic Oncologists, NIH/NCI, 1 T32CA101642-01A, PI - David M. Gershenson, MD, 2005–2010, \$1,535,549 (\$181,757/year), NIH/NCI

Collaborator, A Limited Access Phase II Trial of Cetuximab (C225, NSC 714692) in Combination with Cisplatin (NSC #119875) in the Treatment of Advanced, Persistent, or Recurrent Carcinoma of the Cervix, GOG-0076DD, PI - Robert Coleman, M.D., 2005–2011, GOG

Principal Investigator, A Phase I Trial of Tailored Radiation Therapy with Concomitant Cetuximab (C225, NSC# 714692) and Cisplatin (NSC# 119875) in the Treatment of Patients with Cervical Cancer, GOG-9918, 2005–2011, GOG

Collaborator, A Phase II Evaluation of Pemetrexed (Alimta, LY231514, IND #40061) in the Treatment of Recurrent Carcinoma of the Cervix, GOG-0127T, PI - Charles Levenback, M.D., 2005–2011, GOG

Collaborator, A Phase II Evaluation of Thalidomide (NSC# 66847, IND# 48832) In The Treatment Of Recurrent Or Persistent Carcinosarcoma of the Uterus, GOG-0230B, PI - Lois Ramondetta, M.D., 2006–2007, GOG

Principal Investigator, A Dose-Escalating Phase I Study with an Expanded Cohort to Assess Feasibility of Intraperitoneal Carboplatin & Intravenous Paclitaxel in Patients with Previously Untreated Epithelial Ovarian, Primary Peritoneal, or Fallopian Tube Cancer, GOG-9917, 2006–2011, GOG

Collaborator, A Phase II Evaluation of Pemetrexed (Alimta, LY231514, IND #40061) in the Treatment of Recurrent or Persistent Platinum-Resistant Ovarian or Primary Peritoneal Carcinoma, GOG-0126Q, PI - Siqing Fu, M.D., 2006–2011, GOG

Co-Principal Investigator, A Phase II Study of Faslodex in Recurrent/Metastatic Endometrial Carcinoma, GOG-0188, PI - Lois Ramondetta, M.D., 2006–2011, GOG

Co-Principal Investigator, Phase III Carboplatin & Paclitaxel + Placebo vs. Carboplatin & Paclitaxel + Concurrent Bevacizumab (NSC #704865, IND # 7921) followed by Placebo, vs Carboplatin & Paclitaxel + Concurrent & Ext Bevacizumab, in Advanced Stage Epithelial Ovarian & Peritoneal Primary Cancer, GOG-0218, PI - Robert Coleman, M.D., 2006–2011, GOG

Collaborator, A Phase II Evaluation of ABI-007 (IND #55,974) in the Treatment of Persistent or Recurrent Squamous or Non Squamous Cell Carcinoma of the Cervix (Abraxis BioScience, Inc. Study #CA026) (Group B), GOG-0127V, PI - Robert Coleman, M.D., 2007–2011, GOG

Principal Investigator, Preliminary Evaluation of Femara (Letrozole) for Adjuvant Treatment After Completion of First-Line Chemotherapy for Patients with Optimally Debulked and Chemosensitive Ovarian Cancer, IRB 2006-0689, 2007–2011, \$314,989

Principal Investigator, Randomized Phase 2 Study of MLN8237, an Aurora A Kinase Inhibitor, Plus Weekly Paclitaxel or Weekly Paclitaxel Alone in Patients with Recurrent Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer, Preceded by a Phase 1 Portion in Patients with Ovarian or Breast Cancer, Millennium.

Unfunded

Collaborator, A Phase II Study of Intravenously Administered Tirapazamine Plus Cisplatin in Subjects with Cervical Cancer, GYN96-136, PI - Charles Levenback, M.D., 1996-2004

Principal Investigator, Phase I Study of recurrent ovarian cancer Adp53, ID 97-288, 1997

Collaborator, Telomerase Testing in Peritoneal Washings from Ovarian Cancer Patients Undergoing Second Look Laparotomy, LAB98-080, PI - David Gershenson, M.D., 1998-2005

Collaborator, A Pilot Study of Transfusion of rhTPO-Derived Autologous Platelets Cryopreserved with Thrombocin and 2% DMSO in Patients with Gynecologic Malignancy Receiving Carboplatin, GYN97-310, PI - Saroj Vadhan, 1999-2004

Collaborator, Paclitaxel, Carboplatin, and Herceptin for Patients with Untreated Advanced, (Cohort A) or Recurrent Platinum-Sensitive (Cohort B) Epithelial Ovarian Cancer, Peritoneal Cancer, or Fallopian Tube Cancer, GYN99-067, PI - David Gershenson, M.D., 1999-2004

Collaborator, Paclitaxel, Carboplatin, and Herceptin for Patients with Untreated Advanced Epithelial Ovarian Cancer, Peritoneal Cancer, or Fallopian Tube Cancer, GYN99-132, PI - David Gershenson, M.D., 1999-2007

Collaborator, Feasibility of Measuring Gene Expression Patterns Using Tissue Acquisition of Primary Stage III and IV Epithelial Ovarian Cancer, Fallopian Tube, or Primary Peritoneal Cancer and Gene Expression Array Technology for Predicting Paclitaxel Chemotherapy Sensitivity and Resistance, ID00-408, PI - David Gershenson, M.D., 2000-2011

Principal Investigator, Phase II Study of Paclitaxel for Ovarian Stromal Tumors as First-Line or Second-Line Therapy, GOG-0187, 2000

Collaborator, A Phase II Study of Intraperitoneal E1A-Lipid complex for Patients with Advanced Epithelial Ovarian CX without Her-2/Neu Overexpression, ID00-306, PI - Naoto Ueno, 2001-2002

Collaborator, Phase II Study of Intraperitoneal Recombinant Human Interleukin-12 (RHIL-12) in Patients with Peritoneal Carcinomatosis (Residual Disease <1cm) Associated with Ovarian epithelial CX or Primary Peritoneal Carcinoma, ID00-232, PI - Renato Lenzi, 2001-2005

Collaborator, Feasibility Study of Intraoperative Lymphatic Mapping and Sentinel Lymph Node Identification in Patients with Endometrial Cancer, ID01-290, PI - Diane Bodurka, M.D., 2001-2006

Collaborator, A Phase II Multicenter Trial of Paclitaxel and Carboplatin in Women with Advanced (IIb, IIc, IVa and IVb) or Recurrent (All Stages) Mixed Malignant Mullerian Tumors (MMMT) of the Uterus, ID01-229, PI - Lois Ramondetta, M.D., 2001-2011

Collaborator, A Phase II Study: Paclitaxel and Pelvic Radiation for Stage I-IIIa Papillary Serous Carcinoma of the Endometrium, ID-418, PI - Anuja Jhingran, 2001-2011

Collaborator, Chemotherapy-Related Toxicities in Ovarian Cancer Patients: Preference Assessments of Patients, Family Members, Ancillary Staff and Gynecologic Oncologists, and Patients' Quality of Life, GYN00-409, PI - Diane Bodurka, M.D., 2001-2011

Collaborator, Clinical and Molecular Genetic Determinants of Late Complication in Patients Treated with Radiation Therapy for Cervical Cancer, LAB01-380, PI - Patricia Eifel, M.D., 2001-2011

Collaborator, Evaluating Fatigue and Other Symptoms of Ovarian Cancer Patients with Ecological Momentary Assessment, ID00-013, PI - Karen Basen-Engquist, 2001-2011

Collaborator, Phase II Study of Mifepristone (RU-486) in the Treatment of PR Positive Advanced/Recurrent Endometrial Adenocarcinoma and Low Grade Endometrial Stromal Sarcoma (LGES), ID01-212, PI - Lois Ramondetta, M.D., 2001-2011

Collaborator, Use of the CA125 Algorithm for the Early Detection of Ovarian Cancer in Low Risk Women, ID01-022, PI - Karen Lu, 2001-2011

Co-Principal Investigator, Vacuum-Assisted Closure in the treatment of Gynecologic Oncology Wound Failures, RCR01-156, PI - Pedro Ramirez, 2002-2003

Collaborator, Phase I Trial of Concurrent Weekly CPT-11, Cisplatin, and Radiotherapy for Patients with Newly Diagnosed Stage IIb-IVa Cancer of the Uterine Cervix, ID02-526, PI - Pedro Ramirez, M.D., 2002-2005

Collaborator, A Phase II Study of Chemoimmunotherapy for Patients with Potentially Platinum Sensitive Müllerian (Epithelial Ovarian, Peritoneal, or Fallopian Tube) Carcinomas, ID02-231, PI - Ralph Freedman, M.D., Ph.D., 2002-2011

Collaborator, A Prevalence Study of HNPCC Gene Mutation in Women with Endometrial Cancers, ID01-533, PI - Karen Lu, M.D., 2002-2011

Collaborator, Feasibility of Measuring Gene Expression Patterns Using Tissue Acquisition of Primary Peritoneal CX and Gene Expression Array Technology for Predicting Paclitaxel Chemo Sensitive and Resistant, ID00-408, PI - David M. Gershenson, M.D., 2002-2011

Collaborator, Modulation of Putative Surrogate Endpoint Biomarkers in Endometrial Biopsies from Women with HNPCC, ID01-340, PI - Karen Lu, M.D., 2002-2011

Collaborator, The Utility and Impact of Computed Tomography and Serum CA-125 in the Management of Newly Diagnosed Ovarian Cancer, ID02-143, PI - Pedro Ramirez, M.D., 2002-2011

Co-Principal Investigator, Evaluation of Molecular Markers in Malignant Mixed Mesodermal Tumors (MMMT) of the Ovary, LAB03-0653, PI - Lois Ramondetta, M.D., 2003-2005

Co-Principal Investigator, A Phase I Study Evaluating the Safety and Tolerability of PS-341(Bortezomib) and Carboplatin in Patients with Platinum Resistant Recurrent Ovarian Cancer, Primary Peritoneal Cancer, and Fallopian Tube Cancer, ID02-114, PI - Pedro Ramirez, 2003-2007

Collaborator, Phase III Randomized Study of TLK286 Versus Doxil/Caelyx or Hycamtin as Third-Line Therapy in Platinum Refractory or Resistant Ovarian Cancer, ID03-184, PI - John Kavanagh, M.D., 2003-2007
Co-Principal Investigator, Role of Secondary Cytoreductive Surgery for Recurrent Ovarian: A 20-Year Experience, RCR03-0803, PI - Pedro Ramirez, 2003-2007
Collaborator, A Phase II Study Evaluating the Utility of Letrozole in the Treatment of Recurrent, Estrogen Receptor (ER) Positive, Epithelial Ovarian Cancer, Fallopian Tube Cancer, and Primary Peritoneal Cancer, ID02-698, PI - Pedro Ramirez, M.D., 2003-2011
Collaborator, A Pilot Study of Laparoscopic Extraperitoneal Lymph Node Dissection in Patients with Locally Advanced Cervical Cancer, ID03-0098, PI - Pedro Ramirez, M.D., 2003-2011
Collaborator, Phase 1-2a Dose-Ranging Study of TLK286 in Combination with Doxil in Platinum Refractory or Resistant Ovarian Cancer, ID02-571, PI - John Kavanagh, M.D., 2003-2011
Collaborator, Phase II Study of Letrozole in Patients with Recurrent Advanced Borderline Tumors or Low Grade Epithelial Cancers of the Ovary, Fallopian Tube and Primary Peritoneum, 2003-0486, PI - John Kavanagh, M.D., 2003-2011
Collaborator, Quality of Life and Preferences of Ovarian Cancer Patients Enrolled on a Randomized Trial of High-Dose versus Conventional Dose Chemotherapy, ID02-680, PI - Charlotte Sun, Ph.D., 2003-2011
Co-Principal Investigator, A Phase II Study of Gemcitabine and Cisplatin for Advanced or Recurrent Endometrial Cancer, 2003-0823, PI - Jubilee Brown, M. D., 2004-2011
Collaborator, Chemoradiation-Induced Nausea and Emesis: A Prospective Study to Assess Patient Preferences and Quality of Life, 200-0529, PI - Charlotte Sun, Ph.D., 2004-2011
Collaborator, The Role of Appendectomy at the Time of Tumor Reductive Surgery in Patients with Epithelial Ovarian Cancer, RCR05-0630, PI - Pedro Ramirez, M.D., 2005
Collaborator, Total Laparoscopic Radical Hysterectomy: Outcomes Evaluation, RCR05-0390, PI - Pedro Ramirez, M.D., 2005-2007
Co-Principal Investigator, A Pilot Clinical Trial with Molecular Marker Study of Chemosensitization to Carboplatin by Use of Vidaza in Platinum Resistant or Refractory Epithelial Ovarian Cancer, 2005-0009, PI - Siqing Fu, M.D., 2005-2011
Collaborator, Evaluation of Demographics and Perioperative Care of Patients Undergoing Laparoscopic Surgery for Gynecologic Malignancies: A 15-Year Experience, RCR05-0137, PI - Pedro Ramirez, M.D., 2005-2011
Collaborator, Systemic Antineoplastic Therapy in Ovarian Cancer Patients with Renal Dysfunction, RCR05-0707, PI - John Kavanagh, M.D., 2005-2011
Collaborator, A Phase I Dose Escalation Study of ABI-007 with Carboplatin as First-Line Therapy in Patients with Epithelial Ovarian, Primary Peritoneal, or Fallopian Tube Carcinoma, 2006-0405, PI - Robert Coleman, M.D., 2006-2011
Principal Investigator, Phase II Study of Cetuximab (Erbix) in Patients with Progressive or recurrent Endometrial Cancer, 2006-0211, 2006-2011
Collaborator, A Multi-Institutional Study of Proteomic Evaluation of Epithelial Ovarian Cancer, Primary Peritoneal Cancer, and Fallopian Tube Cancer Patients in First Clinical Remission: Development of a Protein Fingerprint Profile of Relapse, 2005-0780, PI - Karen Lu, M.D., 2007-2011
Co-Principal Investigator, A Phase II, Open-Label, Non-Comparative, International, MC Study to Assess the Efficacy and Safety of KU-0059436 Given Orally Twice Daily in Patients with Advanced BRCA1-or BRCA2-Associated Ovarian Cancer, 2007-0098, PI - Karen H. Lu, M.D., 2007-2011
Collaborator, A Study of the Efficacy of MORAb-003 in Subjects with Platinum-Sensitive Epithelial Ovarian Cancer in First Relapse, 2006-0889, PI - Robert Coleman, M.D., 2007-2011
Collaborator, Phase I/II and Pharmacokinetic Study of Docetaxel Plus VEGF Trap (AVE0005, NSC #724770) In Patients with Recurrent Ovarian, Primary Peritoneal, and Fallopian Tube Cancer, 2006-0329, PI - Robert Coleman, M.D., 2007-2011

Patents and Technology Licenses

Patents

N/A

Technology Licenses

N/A

Grant Reviewer/Service on Study Sections

Review Committee on NIH CTRC, NIH, Member, Louisiana State University, 1997
AD HOC on NCI P01, NCI, Ad Hoc Member, Tulane University Health Science Center, 2004
Clinical Research Review Committee NCI, NCI, Member, Mayo Clinic, 2004
NIH-CONC Clinical Oncology Study Section Review (R01, R21), NIH, Member, Clinical Oncology Study Section Review (R01, R21), San Francisco, CA, 2004
Review Committee NCI-NIH, NIH, Member, Duke Comprehensive Cancer Center, Duke University, 2004
Review Committee on NCI-I Career Awards, NCI, Member, 2004
NCI P01 Cluster Review, NIH, Member, Bethesda, MD, 2005
NIH-CONC Clinical Oncology Study Section Review (R01, R21), NIH, Member, Clinical Oncology Study Section Review (R01, R21), Bethesda, MD, 2005
Review Committee NCI-NIH, P01 Experimental Therapeutics II Cluster Review, NIH, Member, P01 Experimental Therapeutics II Cluster Review, Rockville, MD, 2005

PUBLICATIONS

Peer-Reviewed Original Research Articles

1. Yu D, **Wolf JK**, Scanlon M, Price JE, Hung MC. Enhanced c-erbB-2/neu expression in human ovarian cancer cells correlates with more severe malignancy that can be suppressed by E1A. *Cancer Res* 1993 Feb 15;53(4):891-8.
2. Hamada K, Zhang WW, Alemany R, Roth JA, **Wolf JK**, Mitchell MF. Gene therapy of cervical cancer by adenovirus-mediated p53 gene transfer. *J Cell Biochem Suppl* 1995; 21A:421.

3. Gershenson DM, Morris M, Burke TW, Levenback C, **Wolf JK**, Warner D, Matthews CM, Wharton JT. Treatment of poor-prognosis sex cord-stromal tumors of the ovary with the combination of bleomycin, etoposide, and cisplatin(BEP). *Obstet Gynecol* 1996 Apr;87(4):527-31.
4. **Wolf JK**, Levenback C, Malpica A, Morris M, Burke T, Mitchell MF. Adenocarcinoma in situ of the cervix: significance of cone biopsy margins. *Obstet Gynecol* 1996 Jul; 88(1)(1):82-6.
5. Levenback C, Morris M, Burke TW, Gershenson DM, **Wolf JK**, Wharton JT. Groin dissection practices among gynecologic oncologists treating early vulvar cancer. *Gynecol Oncol* 1996 Jul; 62(1)(1):73-7.
6. Hamada K, Zhang WW, Alemany R, **Wolf JK**, Roth JA, Mitchell MF. Growth inhibition of human cervical cancer cells with recombinant adenovirus p53 in vitro. *Gynecol Oncol* 1996;60(3):373-379.
7. Mitchell MF, Hamada K, Jagannadha S, Satterfield WC, Buchholz S, **Wolf JK**, Zhang WU, Alemany R, Tortolero-Luna G, Keeling ME, Wharton JT, Roth JR. Transgene expression in the rhesus cervix mediated by an adenovirus expressing b-galactosidase. *Am J Obstet Gynecol* 1996;174:1094-1101.
8. Brader KR, **Wolf JK**, Hung MC, Yu D, Crispens MA, van Golen KL, Price JE. Adenovirus E1A expression enhances the sensitivity of an ovarian cancer cell line to multiple cytotoxic agents through an apoptotic mechanism. *Clin Cancer Res* 1997 Nov; 3(11):2017-24.
9. Gershenson DM, Silva EG, Levy L, Burke TW, **Wolf JK**, Tornos C. Ovarian serous borderline tumors with invasive peritoneal implants. *Cancer* 1998 Mar; 82(6)(6):1096-103.
10. Brader KR, **Wolf JK**, Chakrabarty S, Price JE. Epidermal growth factor receptor (EGFR) antisense transfection reduces the expression of EGFR and suppresses the malignant phenotype of a human ovarian cancer cell line. *Oncol Rep* 1998 Sep-Oct; 5(5):1269-74.
11. Price JE, **Wolf JK**, Pathak S. Distinctive karyotypes and growth patterns in nude mice reveal cross-contamination in an established human cancer cell line. *Oncol Rep* 1998 Jan-Feb; 5(1)(1):261-6.
12. **Wolf JK**, Kim TE, Fightmaster D, Bodurka D, Gershenson DM, Mills G, Wharton JT. Growth suppression of human ovarian cancer cell lines by the introduction of a p16 gene via a recombinant adenovirus. *Gynecol Oncol* 1999 Apr; 73(1)(1):27-34.
13. **Wolf JK**, Mullen J, Eifel PJ, Burke TW, Levenback C, Gershenson DM. Radiation treatment of advanced or recurrent granulosa cell tumor of the ovary. *Gynecol Oncol* 1999 Apr; 73(1):35-41.
14. **Wolf JK**, Mills GB, Bazzet L, Bast RC, Roth JA, Gershenson DM. Adenovirus-mediated p53 growth inhibition of ovarian cancer cells is independent of endogenous p53 status. *Gynecol Oncol* 1999 Nov; 75(2)(2):261-6.
15. Gershenson DM, Morris M, Burke TW, Levenback C, **Wolf JK**, Lee JJ, Thall PF, Atkinson EN, Silva EG, Wharton JT. A phase I trial of intravenous melphalan, paclitaxel, and cisplatin plus granulocyte-colony stimulating factor in patients with suboptimal advanced epithelial ovarian carcinoma or peritoneal carcinoma. *Cancer* 1999 Dec;86(11):2291-300.
16. Bodurka-Bervers, Basen-Engquist KM, Fitzgerald MA, Bevers MW, **Wolf JK**, Levenback C, Gershenson DM. Depression may worsen quality of life in patients with epithelial ovarian cancer. *Gynecol Oncol* 1999;72:449.
17. Bodurka-Bervers D, Basen-Engquist K, Carmack CL, Fitzgerald MA, **Wolf JK**, de Moor C, Gershenson DM. Depression, anxiety, and quality of life in patients with epithelial ovarian cancer. *Gynecol Oncol* 2000 Sep; 78(3)(3 Pt 1):302-8.
18. Parker LP, **Wolf JK**, Price JE. Adenoviral-mediated gene therapy with Ad5CMVp53 and Ad5CMVp21 in combination with standard therapies in human breast cancer cell lines. *Ann Clin Lab Sci* 2000 Oct; 30(4)(4):395-405.
19. Gordinier ME, Ramondetta LM, Parker LP, **Wolf JK**, Follen M, Gershenson DM, Bodurka-Bervers D. Survey of female gynecologic oncologists and fellows: balancing professional and personal life. *Gynecol Oncol* 2000 Nov; 79(2)(2):309-14.
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32. Ramirez PT, Modesitt SC, Morris M, Edwards CL, Bevers MW, Wharton JT, **Wolf JK**. Functional outcomes and complications of continent urinary diversions in patients with gynecologic malignancies. *Gynecol Oncol* 2002 May; 85(2)(2):285-91.
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 65. Smith JA, Gaikwad A, Ramondetta LM, **Wolf JK**, Brown J. Determination of the mechanism of gemcitabine modulation of cisplatin drug resistance in panel of human endometrial cancer cell lines. *Gynecol Oncol* 2006 Nov;103(2):518-22.
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 71. Crotzer DR, **Wolf JK**, Gano JB, Gershenson DM, Levenback C. A pilot study of cisplatin, ifosfamide and mesna in the treatment of malignant mixed mesodermal tumors of the ovary. *Gynecol Oncol*. 2007 May; 105(2):399-403. Epub 2007 Feb 9.
 72. Smith JA, Gaikwad A, Yu J, **Wolf JK**, Brown J, Ramondetta L, Stewart C. In vitro evaluation of the effects of gefitinib on the modulation of cytotoxic activity of selected anticancer agents in a panel of human ovarian cancer cell lines. *Cancer Chemother Pharmacol* 62(1):51-58, 2008. e-Pub 9/2007
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- Hung MC. A novel hTERT promoter-driven E1A therapeutic for ovarian cancer. *Mol Cancer Ther*. 2009 Sept;8(8):2771
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83. Fu S, Hu W, Iyer R, Kavanagh JJ, Coleman RL, Levenback CF, Sood AK, **Wolf JK**, Gershenson DM, Markman M, Hennessy BT, Kurzrock R, Bast RC. Phase 1b-2a study to reverse platinum resistance through use of a hypomethylating agent, azacitidine, in patients with platinum-resistant or platinum-refractory epithelial ovarian cancer. *Cancer*. 2011 Apr 15;117(8) e-Pub 2010 Nov 8.
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87. Hunter RJ, Fujii H, Wakame K, Gaokwad A, **Wolf JK**, Smith JA. *In vitro* and *in vivo* evaluation of active hexose correlated compound (AHCC) in combination with pegylated liposomal doxorubicin for treatment of ovarian cancer. *The Journal of Applied Research in Natural Products*. Vol 4, No 3 2011
88. King ER, Tung CS, Tsang YT, Zu Z, Lok GT, Deaves MT, Malpica A, **Wolf JK**, Lu KH, Birrer MJ, Mok SC, Gershenson DM, Wong KK. The anterior gradient homolog 3 (AGR3) gene is associated with differentiation and survival in ovarian cancer. *American Journal of Surgical Pathology*, 2011 Jun, 35(6):904-12.
89. Rahma OE, Ashtar E, Czystowska M, Szajnik ME, Wieckowski E, Bernstein S, Herrin VE, Shams MA, Steinberg SM, Merino M, Gooding W, Visus C, Deleo AB, **Wolf JK**, Bell JG, Berzofsky JA, Whiteside TL, Khleif SN. A Gynecologic Oncology Group Phase II trial of two p53 peptide vaccine approaches: subcutaneous injection and intravenous pulsed dendritic cells in high recurrence risk ovarian cancer patients. *Cancer Immunol Immunother*. 2012 Mar;61(3):373-84. Epub 2011 Sep 17
90. Fu S, Hennessy BT, Ng CS, Ju Z, Coombes KR, **Wolf JK**, Sood AK, Levenback CF, Coleman RL, Kavanagh JJ, Gershenson DM, Markman M, Dice K, Howard A, Li J, Li Y, Stemke-Hale K, Dyer M, Atkinson E, Jackson E, Kundra V, Kurzrock R, Bast RC Jr, Mills GB. Perifosine plus docetaxel in patients with platinum and taxane resistant or refractory high-grade epithelial ovarian cancer. *Gynecol Oncol*. 2012 Jul;126(1):47-53.
91. Julius JM, Tanyi JL, Ramos L, Munsell MF, Watkins JL, Coleman RL, **Wolf JK**, Smith JA. Evaluation of pegylated liposomal doxorubicin dose on the adverse drug event profile and outcomes in treatment of recurrent endometrial cancer. *International Journal of Gynecologic Oncology*. 2013 Feb;23(2):348-54
92. Estrella JS, **Wolf JK**, Deavers MT. Ovarian serous carcinoma associated with a distinct "corded and hyalinized" pattern. *Archives of Pathology and Laboratory Medicine*. 2013 Feb;137(2):275-9.
93. Julius JM, Nogueras-Gonzalez GM, Watkins JL, Coleman RL, **Wolf JK**, Smith JA. Effect of declining renal function on the incidence of adverse drug events associated with liposomal doxorubicin in patients treated for gynecologic malignancies. *International Journal of Gynecologic Oncology*. 2013 Feb;23(2):48-54
94. Robert L. Coleman, MD; Thomas J. Herzog, MD; Daniel W. Chan, PhD; Donald G. Munroe, PhD; Todd C. Pappas, PhD; Alan Smith, MS; Zhen Zhang, PhD; Judith Wolf, MD. Validation of a second-generation multivariate index assay for malignancy risk of adnexal masses. *Am J Obstet Gynecol* 2016;volume;x.x-x.x
95. Ramez N. Eskander, Brian A. Carpenter, Howard G. Wu & Judith K. Wolf (2016) The clinical utility of an elevated-risk multivariate index assay score in ovarian cancer patients, *Current Medical Research and Opinion*, 32:6, 1161-1165, DOI: 10.1080/03007995.2016.1176014

Invited Articles

1. **Wolf JK**, Wharton JT. Wild-type p53 overexpression: what role in tumorigenesis? *Gynecol Oncol* 60(3):337-8, 3/1996.
2. **Wolf JK**. Management of wound complications. *Clin Consults in Ob/Gyn* 8:79-84, 1996.
3. **Wolf JK**, Ramirez PT. The molecular biology of cervical cancer. *Cancer Invest* 19(6):621-9, 2001.
4. **Wolf JK**, Jenkins AD. Gene therapy for ovarian cancer (review). *Int J Oncol* 21(3):461-8, 9/2002.
5. **Wolf JK**, Coleman RL. Commentary on, Phase I trial of intraperitoneal injection of the E1B-55-kd-gene-deleted adenovirus ONYZ-015(d11520) given on days 1 through 5 every 3 weeks in patients with recurrent/refractory epithelial ovarian cancer. Vasey, et al. *J Clin Oncol* 2002;20:1562-9." *Women's Oncol Rev* 2:325-7, 2002.
6. **Wolf JK**, Franco EL, Arbeit JM, Shroyer KR, Wu TC, Runowicz CD, Tortolero-Luna G, Herrero R, Crum CP. Innovations in understanding the biology of cervical cancer. *Cancer S* 98(9):2064-9, 2003.
7. **Wolf JK**, Franco EL, Arbeit JM, Shroyer KR, Wu TC, Runowicz CD, Tortolero-Luna G, Herrero R, Crum CP. Innovations in understanding the biology of cervical cancer. *Cancer S* 98(9)(9 Suppl):2064-9, 2003.
8. Markman, Gershenson DM, **Wolf JK**. Controversies in Ovarian Cancer. *ACOG Update* 30:1-9, 2004.
9. Soliman PT, Slomovitz BM, **Wolf JK**. Mechanisms of cervical cancer. *Drug Discov Today: Dis Mech* 1(2):253-258, 2004.
10. Slomovitz B, Soliman P, **Wolf JK**. New standards for treating recurrent ovarian cancer. *NOCC* 19(Summer):5, 2004.
11. **Wolf JK**, Slomovitz BM. Novel biologic therapies for the treatment of endometrial cancer. *Int J Gynecol Cancer* 15(2):411, 2005.
12. **Wolf JK**. Prevention and treatment of vaginal stenosis resulting from pelvic radiation therapy. *Community Oncol* 3(10):665-71, 2006.

Editorials

1. **Wolf JK**, Wharton JT. Wild-type p53 overexpression: what role in tumorigenesis? *Gynecol Oncol* 60(3):337-8, 1996.

Other Articles

1. **Wolf JK**. Gynecologic Cancer Treatment Update (Highlights from ASCO 2003). *Vital Signs Monograph*, Fall, 2003.
2. Herzog, Coleman R, McGuire, Monk B, Spriggs D, **Wolf JK**. Patterns of Practice in Selected Gynecologic Malignancies. Colloquium at the Annual Meeting on Women's Cancer 2005 36th Annual Meeting of the Society of Gynecologic Oncologist. (SGO Monograph), 2005.

Abstracts (Past 5 years)

1. Jhingran A, Ramondetta L, Bodurka D, Brown J, Eifel P, Garcia M, Lu K, **Wolf JK**, Burke T. A prospective phase II study of chemoradiation followed by adjuvant chemotherapy for stage I-IIIa uterine papillary serous carcinoma. *Gynecologic Oncology* 116(3, S1):S9 (#15), 3/2010.
2. Brown J, Sood A, Ramirez P, Ramondetta L, Coleman R, Levenback C, Jung M, **Wolf JK**. Combination gemcitabine and cisplatin are highly active in endometrial carcinoma: Results of a prospective phase II trial. *Gynecologic Oncology* 116(3, S1) (#49), 3/2010.
3. Wong K, Tsang Y, Zu Z, Mok S, Deavers M, Birrer M, **Wolf JK**, Lu K, Gershenson D. Insulin growth factor 1 pathway is a potential therapeutic target for low-grade ovarian serous carcinomas. *Gynecologic Oncology* 116(3, S1):S113 (#290), 3/2010.
4. Slomovitz B, Schmeler K, Miller D, Lu K, Ramirez P, Caputo T, Coleman R, Burke T, Gershenson D, **Wolf JK**. Phase II study of cetuximab (Erbix) in patients with progressive or recurrent endometrial cancer. *Gynecologic Oncology* 116(3, S1):S8-9 (#13). e-Pub 3/2010.
5. Rahma O, Achta e, Czysowska M, Szajn ME, Wieckowski E, Bernstein S, Herrin VE, Steinert SM, Merino M, Gooding W, Visus C, DeLeo AB, Berzofsky JA, Whiteside TL, **Wolf JK**, Bell JG, Khleif SN. Comparable effect of p53 peptide vaccine in adjuvant or pulsed on dendritic cells in ovarian cancer patients: A gynecologic oncology group study. *Proceedings of the American Association for Cancer Research* 51:585 (#2414), 4/2010.
6. Slomovitz B, Soliman P, Levenback C, Brown J, **Wolf J**, Schmeler K, Johnston T, Mura D, Stone R, Lu K, Coleman R. Everolimus (E) and letrozole (L) in women with previously treated recurrent endometrial cancer(EC): A multiinstitutional phase II clinical trial. (ASCO Submitted 02/2012)
7. Reed K, **Wolf JK**, Deavers MT, Parker L, Schmeler K. Paget's Disease of the Vulva. *Society of Gynecologic Oncologists*, 3/2012
8. Meyer LA, Slomovitz BM, Djordjevic B, Munsell M, Broaddus R, Iglesias DA, Westin SN, Gershenson DM, **Wolf JK**, Lu KH. Can negative biomarkers be helpful? A novel combination test to predict non-response to inhibition of the mammalian target of rapamycin (mTOR) pathway in endometrial cancer. *Society of Gynecologic Oncologists*, 3/2012
9. Fu S, Hennessy BT, Ng CS, Ju Z, Coombes KR, **Wolf JK**, Sood AK, Levenback CF, Coleman RL, Kavanagh JJ, Gershenson DM, Markman M, Dice K, Howard A, Li J, Li Y, Stemke-Hale K, Dyer M, Atkinson E, Jackson E, Kundra V, Kurzrock R, Bast RC Jr, Mills GB. Perifosine plus docetaxel in patients with platinum and taxane resistant or refractory high-grade epithelial ovarian cancer. *American Association for Cancer Research*, 4/2013.

Book Chapters

1. Hallum AV, III, Coleman RL, **Wolf JK**. Gynecologic Oncology. In: The M. D. Anderson Surgical Oncology Handbook. Ed(s) David H. Berger, Barry W. Feig, and George M. Fuhrman. Little Brown and Company: Boston, MA, 326-368, 1995.
2. Bevers MW, Bodurka Bevers DC, **Wolf JK**. Gynecologic Cancers. In: The M. D. Anderson Surgical Oncology Handbook, Second Edition. Ed(s) Barry W. Feig, David H Berger, and George M. Fuhrman. Lippincott Williams & Wilkins: Philadelphia, 377-424, 1998.

3. **Wolf JK**, Mills GB, Bast RC, et al. P53-mediated Gene Therapy. In: Ovarian Cancer. Ed(s) Frank Shart, Tony Blackett, Jonathan Berek and Robert Bast. Isis Medical Media Ltd: Oxford England, 259-27, 1998.
4. **Wolf JK**, Burke TW. Vulva/Vaginal Cancer. In: Practical Strategies in Obstetrics and Gynecology. Ed(s) Mitchell P. Dombrowski, S. Gene McNeeley, Kamran S. Moghissi, and Adnan R. Munkarah. W. B. Saunders Company: Philadelphia, 449-457, 2000.
5. **Wolf JK**. Molecular Biology. In: ACS Atlas of Clinical Oncology: Cancer of the Female Lower Genital Tract. Ed(s) Eifel PJ, Levenback C. B.C. Decker, Inc: Hamilton London, 2001.
6. Bevers MW, Bodurka Bevers DC, **Wolf JK**. Gynecologic Cancers. In: The M. D. Anderson Surgical Oncology Handbook, Third Edition. Ed(s) Barry W. Feig, David H. Berger, and George M. Fuhrman. Lippencott Williams & Wilkins: Philadelphia, PA, 445-490, 2003.
7. Tanyi JL, Crotzer D, **Wolf JK**, Yu S, Hasegawa Y, Lahad J, Wa Cheng K, Umezu-Goto M, Prestwich GD, Morris A, Newman RA, Felix EA, Lapis R, Mills GB. Lysophosphatidic Acid as a Targets for the Molecular Diagnosis and Therapy of Ovarian Cancer. A Review Article. In: Functional Lipidomics. Ed(s) Feng L, Prestwich GD. CRC Press Taylor & Francis Group: Boca Raton, FL, 101-123, 2005.
8. **Wolf JK**, Wharton JT. Surgery for Ovarian Cancer. In: Gynecologic Cancer. Ed(s) Gershenson DM, Eifel PJ, Kavanagh JJ, and Silva E. Springer-Verlag: New York, NY, 174-186, 2005.
9. Slomovitz BM, Soliman PT, **Wolf JK**. Gynecologic Cancers. In: The M. D. Anderson Surgical Oncology Handbook, Fourth Edition. Ed(s) Barry W. Feig, David H. Berger, and George M. Fuhrman. Lippencott Williams & Wilkins: Philadelphia, PA, 520-563, 2006.
10. Smith JA, **Wolf JK**. Ovarian Cancer. In: Pharmacotherapy: A Pathophysiologic Approach 8th Edition, 8th. Ed(s) DiPiro JT, Matzke GR, Yee GC, Talbert RL, Wells BG, Posey LM. McGraw-Hill Companies: Illinois. 2010.

Letters to the Editor

N/A

Manuals, Teaching Aids, Other Teaching Publications

N/A

Other Publications

N/A

EDITORIAL AND REVIEW ACTIVITIES

Editor/Service on Editorial Board(s)

N/A

Member of Editorial Review Board

Editorial Board Member, Clinical Ovarian Cancer: & Other Gynecologic Malignancies, CIG Media, 2008-present

Editorial Board Reviewer, European Journal of Clinical and Medical Oncology, San Lucas Medical Limited c/o Barefoot Investment Ltd, Editorial Board of the Peer Reviewed Journal, 2010-present

Editorial Board Reviewer, American Society of Clinical Oncology, 2013 ASCO Educational Book

Editorial Advisory Board Reviewer, ADC Review/Journal of Antibody-drug Conjugates, 2013

Journal Reviewer

Reviewer, Gynecologic Oncology, 1995-present

Adhoc Reviewer, Obstetrics and Gynecology, 1996-present

Adhoc Reviewer, Clinical Cancer Research, 1998-present

Adhoc Reviewer, International Journal of Gynecologic Cancer, 1998-present

Adhoc Reviewer, International Journal of Radium Oncology, 1998-present

Adhoc Reviewer, Journal of Clinical Oncology, 1999-present

Adhoc Reviewer, American Journal of Pathology, 2001-present

Adhoc Reviewer, American Journal of Obstetrics and Gynecology, 2005-present

Other Editorial and Review Activities

Editor, Help Break the Silence. Talk about Ovarian Cancer, National Ovarian Cancer Coalition - NOCC Editors Event; New York, NY, April 29, 2008

TEACHING

Teaching Within Current Institution – Banner MD Anderson Cancer Center

Formal Teaching

Courses Taught

N/A

Training Programs

N/A

Other Formal Teaching

Lecturer, 1995-1999, Gynecologic Oncology for Enterostomal Therapy Nurses / Role of Gynecologic Oncologist talk given twice a year
1995-1999

Lecturer, 1998, Advances in Research for Ovarian Cancer / Sprint for Life Symposium
1998

Lecturer, 1998, Ovarian Cancer Treatment: Molecular Approaches / Grand Rounds
1998

Lecturer, 1999, Advances and Innovations in Ovarian Cancer / Sprint for Life Symposium

1999

**Supervisory Teaching
Committees**

Advisory Committees

Thesis Advisory Committee, GSBS, Christine Lee, MD, 2001–2003

Thesis Advisory Committee, GSBS, David Crotzer, MD, 2002–2004

Thesis Advisory Committee, GSBS, Monique Nillson, 2003–2005

Supervisory Committees

Chair, Thesis Supervisory Committee, GSBS, David Crotzer, MD, 2002–2004

Examining Committees

N/A

Direct Supervision

Undergraduate and Allied Health Students

N/A

Medical Students

4th Year Medical Students- Midwestern University, Phoenix, AZ

Graduate Students

GSBS, David Crotzer, MD, 2002–2004

Postdoctoral Research Fellows

Tae-Eu Kim Koreai, 1996–1997

Basic Science, Lois Ramondetta, MD, 1998

Basic Science, Pedro Ramirez, MD, 1998

Basic Science, Susan Modesitt, MD, 1999

Basic Science, Veronica Schimp, DO, 2000

Basic Science, Janos Tanyi, 2001–2004

Basic Science, Dwayne Jenkins, MD, 2001

Basic Science, David Crotzer, MD, 2002–2004

Clinical Residents and Fellows

Diljeet Singh, 7/1996–6/1999

Kenny Bozorgi, 7/1996–6/1999

Terri Pustilnik, 7/1996–6/1999

Lois M. Ramondetta, 7/1997–6/2000

Lynn P. Parker, 7/1997–6/2000

Mary E. Gordinier, 7/1997–6/2000

Carlos Herrera, 7/1998–6/2001

Lloyd West, 7/1998–6/2001

Pedro T. Ramirez, 7/1998–6/2001

Jubilee Brown Robinson, 7/1999–6/2002

Matthew Anderson, 7/1999–6/2002

Susan Modesitt, 7/1999–6/2002

Hyun Shvartsman, 7/2000–6/2003

Sean Tedjerati, 7/2000–6/2003

Veronica Schimp, 7/2000–6/2003

Alfred Dwayne Jenkins, 7/2001–6/2004

Amir Jazaeri, 7/2001–6/2004

Jonathan Oh, 7/2001–6/2004

Christine Lee, 7/2001–6/2005

Michael Frumovitz, 7/2001–6/2005

Sachin Apte, 7/2001–6/2005

Brian Slomovitz, 7/2002–6/2006

David Crotzer, 7/2002–6/2006

Premal Thaker, 7/2002–6/2006

Salvador Saldivar, 7/2003–6/2006

Charles Landen, 7/2003–6/2007

Pamela Soliman, 7/2003–6/2007

Aparna Kamat, 7/2004–6/2008

Kathleen Schmeler, 7/2004–6/2008

Liz Han, 7/2004–6/2008

Michael Milam, 7/2005–6/2009

William Merritt, 7/2005–6/2009

Yvonne Lin, 7/2005–6/2009

John Moroney, 7/2006–6/2010

Robin Lacour, 7/2006–6/2010

Shannon Westin, 7/2006–6/2010

Whitney Spannuth, 7/2006–6/2010

Alpa Nick, 7/2007–6/2011

Celestine Tung, 7/2007–6/2011

Larissa Meyer, 7/2007–6/2011

Jennifer Kelly Burzawa, 7/2008–6/2012

Matthew Peter Schlumbrecht, 7/2008–6/2012

Rebecca Lynn Stone, 7/2008–6/2012

Other Supervisory Teaching

Julie Huh, 4th year medical student, Graduate Students, 1996

Lisa Bazzett, Clinical Residents and Fellows, 1997

Mentor, Global Academic Programs - University Hospital Juan Canalejo, Spain, Ovidio Fernandez-Calvo, MD, Foreign Visitor, 2/2009-5/2009

Mentor, Sister Institution Associates - Fudan Cancer Hospital, China, Global Academic Programs, Jie Tang, MD, Foreign Visitor, 6/2009-12/2009

Teaching Outside of Current Institution

Formal Teaching

Courses Taught

Current Directions in Cancer Therapy & Research, National Ovarian Cancer Coalition

Yearly, 1998-present

A-Z Gene Therapy Replacing p53 to achieve antitumor effect, Society of Gynecologic Oncologists

Lecturer, Gene Therapy for Gynecologic Malignancies, University of Texas Medical School

Training Programs

N/A

Other Formal Teaching

N/A

Supervisory Teaching

Committees

Advisory Committees

N/A

Supervisory Committees

PhD Committee, Lee Seabrooke, Arizona State University, Tempe, AZ

Examining Committees

N/A

Direct Supervision

Undergraduate and Allied Health Students

N/A

Medical Students

N/A

Graduate Students

N/A

Postdoctoral Research Fellows

N/A

Clinical Residents and Fellows

N/A

Other Supervisory Teaching

N/A

CONFERENCES AND SYMPOSIA

Organization of Conferences/Symposia (Include chairing session)

N/A

Presentations at National or International Conferences

Invited

Characterization of two populations of the human ovarian cancer cell line, 2774, that express different levels of epidermal growth factor receptor, AACR Annual Meeting, 1993

Characterization of two populations of the human ovarian cancer cell line, 2774, that express different levels of epidermal growth factor receptor, Felix Rutledge Society Annual Meeting, 1993

Enhanced c-erbB-2/neu expression in human ovarian cancer cells correlates with more severe malignancy that can be suppressed by E1A, American Radium Society Annual Meeting, Aruba, 1993

Relationship between expression of c-erbB-2/neu and the malignant phenotype of a human ovarian cancer cell line (SKOV3), Felix Rutledge Society Annual Meeting, 1993

Expression of adenovirus β -galactosidase in rhesus monkey cervix and growth inhibition of human cervical cancer cells by recombinant p53, Felix Rutledge Society Annual Meeting, 1995

Growth inhibition of human ovarian cancer cells by the recombinant adenovirus-mediated transfer of a wild-type p53 gene, Society of Gynecologic Oncologists 26th Annual Meeting, San Francisco, CA, 1995

The significance of cone biopsy margins in patients with adenocarcinoma in situ of the cervix, Felix Rutledge Society Annual Meeting, 1995

A-Z Gene Therapy - Replacing p53 to achieve antitumor effect, Society of Gynecologic Oncologist, 1997

Growth inhibition of human ovarian cancer cells by combination treatment with cisplatin and transfection with adenovirus-mediated p53, Society of Gynecologic Oncologists 28th Annual Meeting, Phoenix, AZ, 1997

Replacing p53 to Achieve an Antitumor Effect, Society of Gynecologic Oncologist 28th Annual Meeting, Phoenix, AZ, 1997

Growth suppression of human ovarian cancer cell lines by the introduction of a P16 via a recombinant adenovirus, Society of Gynecologic Oncologists Annual Meeting, 1998

Cirugia Citorreductora VS Cirugia Minimay uimioterapia Adyuvante, Sociedad Venezolana De Oncologia, VIII Congreso Venezolano De Oncologia, Puerto La Cruz, Venezuela, 10/9/1998

Ganglio Centinela En El Manejo Del Cancer Vulva, Sociedad Venezolana De Oncologia, VIII Congreso Venezolano De Oncologia, Puerto La Cruz, Venezuela, 10/9/1998

Principios De Terapia Genetica Aplicados A Oncologia Media, Sociedad Venezolana De Oncologia, VIII Congreso Venezolano De Oncologia, Puerto La Cruz, Venezuela, 10/9/1998

Terapia Genetica En Cancer, Sociedad Venezolana De Oncologia, VIII Congreso Venezolano De Oncologia, Puerto La Cruz, Venezuela, 10/9/1998

Gene Therapy for Gynecologic Malignancies, Department of Gynecology Grand Rounds, University of Texas Medical School, Houston, TX, 9/28/1999

A phase I trial of ADP53 for ovarian cancer patients: Correlation with p53 and anti-adenovirus AB status, Society of Gynecologic Oncologist Annual Meeting, 2000

A Phase I Trial of Adp53 for Patients with Platinum- and Paclitaxel-Resistant Epithelial Ovarian Cancer, 31st Annual Meeting of the Society of Gynecologic Oncologists, San Diego, CA, 2/9/2000

Prognostic Factors in Endometrial Cancer, Society of Gynecologic Oncologists 2000 Winter Meeting, Park City, UT, 3/18/2000

Effect of Transfecting P16 & P53 Suppressors on Cell Growth and Apoptosis in Ovarian Cancer Cell Lines, American Association for Cancer Research, 91st Annual Meeting, San Francisco, CA, 4/1/2000

Womens Professional Development, Association of American Medical Colleges Professional Development Seminar for Junior Women Faculty, Association of American Medical Colleges, Reston, VA, 4/1/2000

A Phase I Trial of Adp53 (RPR/INGN 201) for Ovarian Cancer Patients: Correlation with P53 and Anti-Adenovirus Antibody Status, American Society of Clinical Oncology, New Orleans, LA, 5/22/2000

Gene Therapy in Patients with Epithelial Ovarian Cancer, Gynecologic Oncology Group, 7/2000

Application of Molecular Biology in Gynecologic Cancer, Annual Meeting of the Thai Gynecologic Oncology Group, Nakorn Nayok, Thailand, 8/12/2000

The Role of Liposomal Doxorubicin (Caelyx) in Ovarian Cancer, Annual Meeting of the Thai Gynecologic Oncology Group, Nakorn Nayok, Thailand, 8/12/2000

Gene Therapy for Cervical Cancer - An Update, 2nd Annual International Conference on Cervical Cancer, Houston, TX, 4/13/2002

In Vivo Adenovirus-Mediated p16 Tumor Suppressor Gene Therapy in Ovarian Cancer, Texas Forum on Female Reproduction 8th Annual Meeting, Houston, TX, 5/2/2002

A Phase II Study of Xeloda in Patients with Chemotherapy Resistant Recurrent Ovarian Cancer, ASCO 2002 Annual Meeting, Orlando, FL, 5/19/2002

The Role of Docetaxel in Gynecologic Malignancies, 40th Japanese Society of Clinical Oncology Annual Meeting, Juntendo University, Tokyo, Japan, 10/16/2002

Management of Ovarian cancer in the 21st Century-Surgery, Chemotherapy, and Molecular Therapy, 40th Japanese Society of Clinical Oncology Annual Meeting, Jutendo University, Tokyo, Japan, 10/17/2002

Surgical Management of Gynecologic Malignancies, 40th Japanese Society of Clinical Oncology Annual Meeting, Jutendo University, Tokyo, Japan, 10/17/2002

A Phase I/II Study to Evaluate the Optimum Biologic Dose of PEG-Intron in Patients with Platinum-Resistant Ovarian, Peritoneal, or Fallopian Tube Cancer, 11th SPORE Investigators Workshop, Baltimore, WA, 7/8/2003

A Phase I/II Study to Evaluate the Optimum Biologic Dose of PEG-Intron in Patients with Platinum-Resistant Ovarian, Peritoneal, or Fallopian Tube Cancer, 11th SPORE Investigator's Workshop, Baltimore, MD, 7/9/2003

P53 Targeted Therapy, 4th International Ovarian Cancer Conference, MSKCC, New York, NY, 9/11/2003

mTOR inhibition is a rational target for the treatment of endometrial cancer, ASCO 40th Annual Meeting, New Orleans, LA, 6/5/2004

Cervical and Endometrial Cancers - Preferred Treatment and Management Options, CME Conference, Hoag Cancer Center, Huntington Beach, CA, 1/28/2005

Health issues and risk factors for Breast and Gynecologic Cancers, Hadassah Check it Out program, San Antonio, TX, 2/9/2005

Cervical Cancer, Ovarian Cancer:What We Need to Know, Women's Health On Alert, Wellesley College, Wellesley, MA, 4/2/2005

Wiley, Miryam (Townsmen Correspondent) Women and hormonal health the expert views., The Wellesley Townsman: townonline.com, Wellesley College, Wellesley, MA, 4/7/2005

Transitioning form Fellow to Faculty: How to go About Setting up an Independent Laboratory, and How to be a Mentor for Students, Residents and Fellows, 2005 Southern Regional Professional Development Conference - Successful Strategies for Women in Academic Medicine, Little Rock, AR, 4/16/2005

The Role of COUP-TFII in Ovarian Cancer, Grand Rounds, Baylor College of Medicine, Houston, TX, 5/6/2005

Biologic Therapies Should be Used as Single Agents in Ovarian Cancer Clinical Trials, Felix Rutledge Society 36th Annual Meeting, Mackinac Island, MI, 7/15/2005

Surgical Treatment of Ovarian Cancer Indications and Advances in the 21st Century, Chinese Society of Gynecologic Oncology, Tsinghua University, Nanjing, China, 6/3/2006

Surgical Treatment of Ovarian Cancer Indications and Advances in the 21st Century and Beyond, International Forum on the Mechanisms and Management of Ovarian Cancer, Peking University People's Hospital, Beijing, China, 6/9/2006

Thymidine Kinase Inh bitors in Gynecologic Malignancies, Felix Rutledge Society 36th Annual Meeting, Berlin, Germany, 9/7/2006

Intraperitoneal Chemotherapy for Optimally Debulked Ovarian Cancer and Emerging Therapies in Ovarian Cancer, 6th Samsung Medical Center - M. D. Anderson Cancer Center International Symposium, Seoul, Korea, Republic of, 11/4/2006

Ovarian Carcinoma for the General Oncologist, Third Symposium, Pursuit of Excellence: Addressing Issues and Trend in Oncology Nursing, UT M D Andersons Physicians Network, Santa Barbara, CA, 7/13/2007

Early Detection and Treatment of Ovarian Cancer, SGO, Tampa, FL, 3/9/2008

Optimizing Treatment Choices in Ovarian Cancer, SGO, Tampa, FL, 3/9/2008

Advances in the Management of Ovarian Stromal Tumors, ASCO, Chicago, IL, 5/31/2008

Ovarian Cancer, Uterine Cancer, Cervical Cancer, Hospital Israelita Albert Einstein and M D Anderson Cancer Center, Hospital Israelita Albert Einstein and M D Anderson Cancer Center, Sao Paulo, Brazil, 6/17/2008

Minimally Invasive Surgery in Gynecology Oncology, II International Symposium of Gynecology Oncology - Hospital Sirio-L banes, Sao Palo, Brazil, 11/7/2008

Gene Therapy and Targeted Therapies in Gynecologic malignancies, II International Symposium of

Gynecology Oncology - Hospital Sirio-Libanês, São Paulo, Brazil, 11/8/2008
Gynecologic Cancers. What you need to know about Ovarian, Uterine, and Cervix Cancers, Albert Einstein Instituto Israelita de Ensino e Pesquisa, São Paulo, Brazil, 6/23/2009
Course Director, 8th International Conference on Ovarian Cancer, Memorial Sloan-Kettering Cancer Center, New York, NY, 9/24/2009
Treatment of Ovarian Cancer 21st Century and Beyond, 6th Chinese Conference on Oncology and the 9th Cross-Strait Conference on Oncology, Fudan University Shanghai Cancer Center, Shanghai, China, 5/21/2010

Chemotherapy Session Moderator, The 9th International Conference on Ovarian Cancer, Houston, TX
12/2/2011

Scientific Exhibitions

Current Directions in Cancer Therapy & Research, Cancer in Women: A Comprehensive Scientific Symposium on the Gynecologic Malignancies, National Ovarian Cancer Coalition, San Diego, CA, 2/4/2000
The Role of Gemcitabine in Ovarian Cancer, Lilly Oncology Advisory Meeting, Indianapolis, IN, 2/28/2002
Current and New Treatment Strategies for Ovarian Cancer, Grand Rounds, University of Medicine & Dentistry of New Jersey, Newark, NJ, 3/27/2002
Challenging Cases in Gynecologic Oncology, Network for Oncology Communication & Research, Las Vegas, NV, 8/17/2002
Cancer in Women: A scientific update in prevention, screening, treatment and risk management for ovarian and cervical malignancies, National Ovarian Cancer Coalition, Inc., Boston, MA, 10/10/2002
Ethical Dilemmas in Clinical Trials, John J. Molitor Lectureship CME Conference, University of California, Irvine, CA, 10/30/2002
The Application of Gene Therapy for Gynecologic Malignancies, Texas Medical Center Gene Therapy Symposium, Houston, TX, 11/11/2002
Indication for and Value of Screening for Ovarian Cancer, CME Conference, Inova Institute of Research & Education, Fairfax, VA, 11/15/2002
Treatment of recurrent Ovarian Cancer, Grand Rounds, Walter Reed Army Medical Center, Bethesda, MD, 12/4/2002
Current Treatment Strategies for Gynecologic Cancers, SGO Symposium 34th Annual Meeting, New Orleans, LA, 2/2/2003
Panel Physician - Ovarian Cancer Panel, The National Comprehensive Cancer Network on Ovarian Cancer Panel, Chicago, IL, 2/7/2003
Novel Therapeutics for Endometrial Cancer, 2003 SGO Winter Meeting, Breckenridge, CO, 3/7/2003
Novel Approaches to the Treatment of Gynecological Cancer, 2003 Oncology Forum, Fox Chase Cancer Center, Philadelphia, PA, 4/26/2003
Satellite Broadcast, Highlights from ASCO 2003, American Academy of the CME, Inc., Newark, NJ, 6/18/2003
What's New in Ovarian Cancer Treatment, NOCC National Conference, Ft. Lauderdale, FL, 11/8/2003
Ovarian Cancer: A Progress Report, 4th Annual Primary Care and Prevention conference, Atlanta, GA, 10/25/2004
Current & New Treatments for Ovarian Cancer, NOCC Conference, Philadelphia, PA, 10/30/2004
Clinical Trials, NOCC National Meeting, Ft. Lauderdale, FL, 11/13/2004
Cancer in Women: a Scientific Update on Ovarian Cancer-Prevention, Screening and Treatment, CME Conference, CME Massachusetts Medical Society & NOCC, 2/4/2005
Phase II Trials among the Ovarian SPORE Programs, Ovarian State of the Science Meeting - GOG Retreat, Bethesda, MD, 9/15/2005
Challenging Cases in Women's Health Recurrent Ovarian Cancer at 8 Months, NMCR Challenging Cases in Gyn Oncology and Breast Cancer, Miami, FL, 6/17/2006
How to Survive and Thrive as a Female Physician in Gynecologic Oncology, Japanese Society of Gynecologic Oncology 42nd Annual Meeting, Tokyo, Japan, 6/28/2007
What's New Gynecologic Oncology? An Update on Translational and Clinical Research, Japanese Society of Gynecologic Oncology 42nd Annual Meeting, Tokyo, Japan, 7/2/2007
Ovarian Carcinoma for the General Oncologist, UT M D Anderson Cancer Center and M D Anderson Physicians Network 3rd Annual Symposium
The University of Texas MD Anderson Cancer Center, Santa Barbara, CA, 7/9/2007 Ovarian Expert Recap - Clinical Options, ASCO, Chicago, IL, 5/30/2008 Controversial Issues in Recurrent Ovarian Cancer, Felix

Rutledge Society Meeting, Buenos Aires, Argentina, 4/29/2009

Conversations with Oncology Investigators, Bridging the Gap between Research and Patient Care,
Research to Practice CME Program, 01/2013

National Seminar Invitations

Attended, Association of American Medical Colleges Professional Development Seminar for Junior
Women Faculty, Reston, Virginia, April 1-4, 2000

Gynecologic Cancers 2003 Treatment Update, CHRISTUS Spohn Shoreline Tumor Conference-CME,
CHRISTUS Spohn Shoreline, Corpus Christi, TX, 8/27/2003

Update in the Management of Ovarian Cancer, Symposium on Women's Cancer, The Cleo Craig
Memorial Cancer and Research Clinic, Lawton, OK, 8/28/2004

Palliative Care Issues for Patients Facing Advanced Ovarian Cancer, MDACC Physicians Network,
Christus Schumpert Cancer CME Symposium, MDACC Physicians Network, Christus Schumpert Cancer
CME Symposium, Shreveport, LA, 10/22/2004

PV, The Abnormal Pap Smear, and Cervical Cancer, MDACC Physicians Network, Christus Schumpert
Cancer CME Symposium, MDACC Physicians Network, Christus Schumpert Cancer CME Symposium,
Shreveport, LA, 10/22/2004

Metastatic Cervical Cancer, Cancer 2005: Preferred Treatment and Management Options, Hoag Cancer
Center CME Oncology Meeting, Huntington Beach, CA, 1/28/2005

Recurrent Endometrial Cancer, Cancer 2005: Preferred Treatment and Management Options, Hoag
Cancer Center CME Oncology Meeting, Huntington Beach, CA, 1/28/2005

Clinical Trials - Understanding, Navigating & Accessing Clinical Trials, Georgia Ovarian Cancer
Awareness Conference, Georgia Ovarian Cancer Awareness Conference, Atlanta, GA, 2/19/2005

Cervical Cancer, Ovarian Cancer: What We Need to Know, Women's Health on Alert, Wellesley College,
Wellesley, MA, 4/2/2005

Recurrent Endometrial Cancer Case#5, Challenging Cases in Women's Health, NOCR, Las Vegas, NV,
8/6/2005

Breaking Sound Barriers: Cutting Edge Research from the Lab and Clinical Trials, Turn the Volume Up-
Ovarian Cancer National Alliance Conference, NOCC, Atlanta, GA, 9/29/2005

Clinical Trials 101, Turn the Volume Up-Ovarian Cancer National Alliance Conference, NOCC, Atlanta,
GA, 9/29/2005

Risk Factors and Genetic Risk factors Regarding Ovarian Cancer, Diagnosis and Treatment of Ovarian
Cancer - Beyond Chemotherapy National Ovarian Cancer Coalition Symposium, NOCC, Philadelphia,
PA, 10/29/2005

Clinical Trials, National Ovarian Cancer Coalition Mini-Conferences, NOCC, Silver Springs, MD,
11/12/2005

Current & New Treatments for Ovarian Cancer, Grand Rounds, Advocate Christ Medical Center, Oak
Lawn, IL, 1/12/2006

Progress and Treatment for Ovarian Cancer, Grand Rounds CME, MacNeal Hospital, Berwyn, IL,
4/25/2006

Women and Cancer: A Focus on Cervical and Ovarian Cancer, Oncology Nursing and Pharmacy
Conference Series 2006: Collaboration for Advancing the Quality of Community Cancer Care, UTMB
Office of Continuing Education, San Diego, CA, 11/18/2006

Women and Cancer: A Focus on Cervical and Ovarian Cancer, Oncology Nursing and Pharmacy
Conference Series 2006: Collaboration for Advancing the Quality of Community Cancer Care, UTMB
Office of Continuing Education, Williamsburg, VA, 12/2/2006

Future Directions and New Frontiers in Individualized Therapeutic Approaches, SGO-CME Certified
Satellite Symposium Management of Recurrent Epithelial Ovarian Cancer: Current Standards and Novel
Approaches, Society of Gynecologic Oncologist, San Diego, CA, 3/5/2007

Treatment of a Patient with Recurrent, Platinum-Resistant Disease, SGO-CME Certified Satellite
Symposium Management of Recurrent Epithelial Ovarian Cancer: Current Standards and Novel
Approaches, Society of Gynecologic Oncologist, San Diego, CA, 3/5/2007

Northwestern Prentice Women's Hospital, Guest Speaker, Chicago, IL. 02/08/2008 "From Bench to
Bedside – My Personal Experience

Texas Medical Association, Ovarian Cancer Advisory Panel Meeting, Austin, TX, July 21, 2008

EIF Callaway Golf Foundation Women's Cancer Initiative Annual Meeting, "Ovarian Cancer Research
Program", Carlsbad, CA, August 8, 2008

The Impact of Stress, Gynecologic Cancer Foundation, NYU Langone Medical Center, New York, NY,
11/1/2008

Global Academic Programs (formerly Sister Institution Conference MDACC), Chair the Working Group on
Gynecologic Malignancies, Houston, TX, 6/6/2008

M D Anderson Cancer Center Development Symposium, accompanied Dr. Mendelsohn and spoke at the

Southern Hills Country Club, Tulsa, OK, June 24, 2008

Gastrointestinal Cancer Retreat and PI3K Workshop: CCSG Programs Onstead Auditorium, BSRB Mitchell Building

Advisor, Entereg Complex Gynecologic Surgery Advisory Meeting, GSK, Philadelphia, PA, December 5-6, 2008

Texas Medical Association, Ovarian Cancer Advisory Panel Meeting, Austin, TX, January 9, 2009

Advisor, Yondelis Advisory Board Meeting, Centocor Ortho Biotech, Newport Beach, CA, February 20-21, 2009

Texas Medical Association, Ovarian Cancer Advisory Panel Meeting, Austin, TX, July 14, 2009

Career Pathways for Women in Science and Medicine & What the Careers of the Future Will Hold and More, Dinner with the Experts, Spring Branch Independent School District, Houston, TX, January 21, 2010

Faculty, CE-Continuing Education Program, OncoBeat ASCO 2010: Reporting the News. Beating Cancer. Educational Concepts Group, LLC; Chicago, IL; June 7, 2010.

Advanced Ovarian Cancer, Facilitator for Interactive Case Discussions, SGO, March 26, 2012

Guest Speaker, "The Ethics of Clinical Trials", Phoenix Chapter of Association of Clinical Research Professionals, July 2013

Lectureships/Visiting Professorships

Gynecologic Oncology Overview, Grand Rounds, Beaumont Hospital, Beaumont, TX, 4/17/1997

Abnormal Uterine Bleeding & Endometrial Cancer, Grand Rounds, St. Frances Cabrini Hospital, Alexandria, LA, 8/24/1999

Gynecologic Oncology Overview, Grand Rounds, Nacogdoches/San Augustine Medical Society, Nacogdoches, TX, 11/10/1999

Gene Therapy for Gynecologic Malignancies, University of Minnesota Fellowship Program, Minneapolis, MN, 12/14/1999

Gynecologic Cancers: Diagnosis, Treatment & Outcomes-Where We've Been & Where We're Going, Grand Rounds, Christus Spohn Health System Tumor Conference, Corpus Christi, TX, 9/20/2000

Current and New Treatment Strategies for Ovarian Cancer, CME, University of Medicine & Dentistry of New Jersey, Medical School, Newark, NJ, 3/27/2002

Ethical Dilemmas in Clinical Trials, John J. Molitor Lectureship, University of California, Irvine, CA, 10/30/2002

The Application of Gene Therapy for Gynecologic Malignancies, Texas Medical Center Gene Therapy Symposium, Texas Medical Center, Houston, TX, 11/11/2002

Indication for and Value of Screening for Ovarian Cancer, CME, Inova Institute of Research & Education, Fairfax, VA, 11/15/2002

Treatment of recurrent Ovarian Cancer, CME, Walter Reed Army Medical Center, Bethesda, MD, 12/4/2002

Novel Therapeutics for Endometrial Cancer, 2003 SGO Winter Meeting, Society of Gynecologic Oncologist, Breckenridge, CO, 3/7/2003

Physician Advisor for Gynecological Cancer Advisory Board, Novel Approaches to the Treatment of Gynecological Cancer, 2003 Oncology Forum, Fox Chase Cancer Center, Philadelphia, PA, 4/26/2003

Translational Research from Bench to Bedside One Gynecologic Oncologist's Experience, Bench to Bedside Symposium, NYU Medical Center, New York, NY, 5/20/2005

Progress and Treatment of Ovarian Cancer, MDACC Faculty Speakers Bureau, CME - OB/GYN Grand Rounds, St. David's Healthcare, Austin, TX, 10/18/2005

Progress and Treatment of Ovarian Cancer, MDACC Faculty Speakers Bureau, CME - University Hospital Grand Rounds, University Health Care System, Augusta, GA, 10/20/2005

Current and New Treatments for Ovarian Cancer, CME, Advocate Christ Hospital, Oak Lawn, IL, 1/12/2006

The Ethics of Clinical Trials, University of Minnesota Gynecologic Oncology Consensus Conference, University of Minnesota, Minneapolis, MN, 5/8/2006

Comprehensive Management of Ovarian Cancer: Current Treatment and Maximizing Quality of Life, CME-Medical Communications Media, Novato Community Hospital, Novato, CA, 5/7/2007

Comprehensive Management of Ovarian Cancer: Current Treatment and Maximizing Quality of Life, Grand Rounds-Medical Communications Media, University of Pittsburgh, Pittsburgh, PA, 6/5/2007

Treatment of Ovarian Cancer - 21st Century and Beyond, Grand Rounds, UC Davis Medical Center, Gynecologic Oncology, Sacramento, CA, 12/17/2008

Gynecologic Cancers: Uterine Cancer, CME: Update on Endometrial Cancer, Citizens Medical Center, Office of Continuing Medical Education, Victoria, TX, 1/11/2010

NATIONAL CONFERENCES- INVITED/ AND OR SPEAKER

Treatment of Ovarian Cancer, National Ovarian Cancer Coalition State Chapters Meeting, NOCC, Ft. Lauderdale, FL, 11/5/1999

Commencement speaker, East Liverpool High School, East Liverpool, OH, 6/1/2000

Gynecologic Cancers: Diagnosis, Treatment & Outcomes-Where We've Been & Where We're Going, 2nd Annual "Closing Gaps & Opening Doors Conference for Working Women, U.S. Department of Labor, Women's Bureau Region VI, Austin, TX, 10/5/2000

Talk-back Session - Moderator, Wet State Theater, Alley Theater, UT M D Anderson Cancer Center & the Stanford Foundation, Austin, TX, 5/31/2001

Interferon-g in the Management of Ovarian Cancer clinical Advisory Program, Advisory Program, InterMune Pharmaceuticals, Houston, TX, 6/21/2001

Current & New Treatments for Ovarian Cancer, Cancer in Women: A Scientific Update in Prevention, Screening and Treatment for Ovarian Cancer, NOCC, Houston, TX, 1/1/2004

Management of Gynecologic Cancer, Sanofi-Synthelabo Oncology Health Science Advisory Board Meeting, Sanofi-Synthelabo Oncology, Dallas, TX, 4/24/2004

Controversies in Ovarian Cancer, ACOG Update, Audiotaped Tele-Conference, ACOG, Houston, TX, 5/14/2004

Health issues and risk factors for Breast and Gynecologic Cancers, Hadassah Check it Out program to educate young women in Houston Independent School District, Worthing High School, Houston, TX, 2/9/2005

Screening for Gynecologic Cancers, CME Memorial Hermann Southwest Hospital, Memorial Hermann Southwest Hospital, Houston, TX, 3/8/2005

The Role of COUP-TFII in Ovarian Cancer, Arthur M. Faris, Sr., MD Resident Research Day, Baylor College of Medicine, Obstetrics and Gynecology, Houston, TX, 5/6/2005

Menopause The Musical Out Loud - Breaking the Silence on Ovarian Cancer, National Ovarian Cancer Coalition, Matrix Graphix, and Ovarian Cancer National Alliance Aging Out Loud Tour, TOC Productions Inc., www.menopausethemusical.com, National Ovarian Cancer Coalition, Stafford, TX, 3/3/2006

Progress and Treatment of Ovarian Cancer, National Ovarian Cancer Coalition, American Cancer Society, National Ovarian Cancer Coalition, American Cancer Society, Austin, TX, 3/20/2006

What you need to know - Hereditary Breast and Ovarian Cancer, UT M D Anderson Cancer Center and The San Antonio Chapter of Hadassah, San Antonio, TX, 10/26/2006

Progress and Treatment for Ovarian Cancer, UTMB - CME Grand Rounds, Galveston, TX, 2/14/2007

Moderator - Stump the Professor, 37th Annual Meeting of the Felix Rutledge Society, Houston, TX, 6/13/2007

Ovarian Cancer Advisory Panel, Physician Oncology Education Program, Ovarian Cancer Advisory Panel Meeting, Texas Medical Association, Austin, TX, 12/10/2007

Cervical Cancer Update Including the Role of Vaccines, SGO-Society of Gynecologic Oncologist, Educational Concepts Group, LLC, Oncobeat SGO: Reporting the News.Beating Cancer, San Antonio, TX, 2/8/2009

Wolf, JK. Strategies for the Management of Platinum-Resistant Ovarian Cancer, 41st Annual Meeting on Women's Cancer Society of Gynecologic Oncologist, CBCE - University of North Texas Health Science Center at Fort Worth, Center for Biomedical Continuing Education, San Francisco, CA, 3/15/2010

Ovarian Cancer, Women's Cancer Awareness Conference, Methodist Healthcare System, San Antonio, TX, 9/30/2010

Gynecologic Oncology Overview, Grand Rounds, Beaumont Hospital, Beaumont, TX, 4/17/1997
Abnormal Uterine Bleeding & Endometrial Cancer, Grand Rounds, St. Frances Cabrini Hospital, Alexandria, LA, 8/24/1999

Gynecologic Oncology Overview, Grand Rounds, Nacogdoches/San Augustine Medical Society, Nacogdoches, TX, 11/10/1999

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Gynecologic Cancers: Diagnosis, Treatment & Outcomes-Where We've Been & Where We're Going, 2nd Annual "Closing Gaps & Opening Doors Conference for Working Women, U.S. Department of Labor, Women's Bureau Region VI, Austin, TX, 10/5/2000

Gynecologic Cancers: Diagnosis, Treatment & Outcomes-Where We've Been & Where We're Going, Grand Rounds, Christus Spohn Health System Tumor Conference, Corpus Christi, TX, 9/20/2000

Talk-back Session - Moderator, Wet State Theater, Alley Theater, UT M D Anderson Cancer Center & the Stanford Foundation, Austin, TX, 5/31/2001

Interferon-g in the Management of Ovarian Cancer clinical Advisory Program, Advisory Program, InterMune Pharmaceuticals, Houston, TX, 6/21/2001

Current and New Treatment Strategies for Ovarian Cancer, CME, University of Medicine & Dentistry of New Jersey, Medical School, Newark, NJ, 3/27/2002

Ethical Delima's in Clinical Trials, John J. Molitar Lectureship, University of California, Irvine, CA,

10/30/2002

The Application of Gene Therapy for Gynecologic Malignancies, Texas Medical Center Gene Therapy Symposium, Texas Medical Center, Houston, TX, 11/11/2002

Indication for and Value of Screening for Ovarian Cancer, CME, Inova Institute of Research & Education, Fairfax, VA, 11/15/2002

Treatment of recurrent Ovarian Cancer, CME, Walter Reed Army Medical Center, Bethesda, MD, 12/4/2002

Novel Therapeutics for Endometrial Cancer, 2003 SGO Winter Meeting, Society of Gynecologic Oncologist, Breckenridge, CO, 3/7/2003

Physician Advisor for Gynecological Cancer Advisory Board, Novel Approaches to the Treatment of Gynecological Cancer, 2003 Oncology Forum, Fox Chase Cancer Center, Philadelphia, PA, 4/26/2003

Current & New Treatments for Ovarian Cancer, Cancer in Women: A Scientific Update in Prevention, Screening and Treatment for Ovarian Cancer, NOCC, Houston, TX, 1/1/2004

Management of Gynecologic Cancer, Sanofi-Synthelabo Oncology Health Science Advisory Board Meeting, Sanofi-Synthelabo Oncology, Dallas, TX, 4/24/2004

Controversies in Ovarian Cancer, ACOG Update, Audiotaped Tele-Conference, ACOG, Houston, TX, 5/14/2004

Health issues and risk factors for Breast and Gynecologic Cancers, Hadassah Check it Out program to educate young women in Houston Independent School District, Worthing High School, Houston, TX, 2/9/2005

Screening for Gynecologic Cancers, CME Memorial Hermann Southwest Hospital, Memorial Hermann Southwest Hospital, Houston, TX, 3/8/2005

The Role of COUP-TFII in Ovarian Cancer, Arthur M. Faris, Sr., MD Resident Research Day, Baylor College of Medicine, Obstetrics and Gynecology, Houston, TX, 5/6/2005

Translational Research from Bench to Bedside One Gynecologic Oncologist's Experience, Bench to Beside Symposium, NYU Medical Center, New York, NY, 5/20/2005

Progress and Treatment of Ovarian Cancer, MDACC Faculty Speakers Bureau, CME - OB/GYN Grand Rounds, St. David's Healthcare, Austin, TX, 10/18/2005

Progress and Treatment of Ovarian Cancer, MDACC Faculty Speakers Bureau, CME - University Hospital Grand Rounds, University Health Care System, Augusta, GA, 10/20/2005

Current and New Treatments for Ovarian Cancer, CME, Advocate Christ Hospital, Oak Lawn, IL, 1/12/2006

Menopause The Musical Out Loud - Breaking the Silence on Ovarian Cancer, National Ovarian Cancer Coalition, Matrix Graphix, and Ovarian Cancer National Alliance Aging Out Loud Tour, TOC Productions Inc., www.menopausethemusical.com, National Ovarian Cancer Coalition, Stafford, TX, 3/3/2006

Progress and Treatment of Ovarian Cancer, National Ovarian Cancer Coalition, American Cancer Society, National Ovarian Cancer Coalition, American Cancer Society, Austin, TX, 3/20/2006

The Ethics of Clinical Trials, University of Minnesota Gynecologic Oncology Consensus Conference, University of Minnesota, Minneapolis, MN, 5/8/2006

What you need to know - Hereditary Breast and Ovarian Cancer, UT M D Anderson Cancer Center and The San Antonio Chapter of Hadassah, San Antonio, TX, 10/26/2006

Progress and Treatment for Ovarian Cancer, UTMB - CME Grand Rounds, Galveston, TX, 2/14/2007
Comprehensive Management of Ovarian Cancer: Current Treatment and Maximizing Quality of Life, CME-Medical Communications Media, Novato Community Hospital, Novato, CA, 5/7/2007

Comprehensive Management of Ovarian Cancer: Current Treatment and Maximizing Quality of Life, Grand Rounds-Medical Communications Media, University of Pittsburgh, Pittsburgh, PA, 6/5/2007

Moderator - Stump the Professor, 37th Annual Meeting of the Felix Rutledge Society, Houston, TX, 6/13/2007

Ovarian Cancer Advisory Panel, Physician Oncology Education Program, Ovarian Cancer Advisory Panel Meeting, Texas Medical Association, Austin, TX, 12/10/2007

Lecturer: Teal Lunch for Life, "Ovarian Cancer: Top Ten Questions What you really need to know..," benefiting Blanton-Davis Ovarian Cancer Research Program, San Antonio, TX, September 10, 2008

Lecturer: E2 Communications-Opinions in Gyn Malignancies: An Interactive Forum and KOL Focus Group, Las Vegas, NV, October 18, 2008

Treatment of Ovarian Cancer - 21st Century and Beyond, Grand Rounds, UC Davis Medical Center, Gynecologic Oncology, Sacramento, CA, 12/17/2008

Lecturer: Shell Health - Shell Oil Company, Prevention and Gynecological Oncology, Houston, TX, April 6, 2009

Lecturer: Raising Ovarian Cancer Awareness to Increase Survival Rates; NOCC, Media Blitz in New York, NY, April 22-23, 2009

Speaker, Teal Lunch for Life, "Ovarian Cancer: What you need to know and how you can help..,"

benefiting Blanton-Davis Ovarian Cancer Research Program, San Antonio, TX, Sept. 9, 2009

Speaker, Key to the Cure Benefit, "Ovarian Cancer, Raise Awareness"; NOCC & Saks 5th Avenue-Austin, Austin, TX, September 17, 2009

Cervical Cancer Update Including the Role of Vaccines, SGO-Society of Gynecologic Oncologist, Educational Concepts Group, LLC, Oncobeat SGO: Reporting the News.Beating Cancer, San Antonio, TX, 2/8/2009

Gynecologic Cancers: Uterine Cancer, CME: Update on Endometrial Cancer, Citizens Medical Center, Office of Continuing Medical Education, Victoria, TX, 1/11/2010

Speaker, CME/CNE Ovarian Cancer Knowledge Video, Texas Medical Association, Ovarian Cancer Advisory Panel Meeting, Austin, TX, January 25, 2010

Wolf, JK. Strategies for the Management of Platinum-Resistant Ovarian Cancer, 41st Annual Meeting on Women's Cancer Society of Gynecologic Oncologist, CBCE - University of North Texas Health Science Center at Fort Worth, Center for Biomedical Continuing Education, San Francisco, CA, 3/15/2010

Ovarian Cancer, Women's Cancer Awareness Conference, Methodist Healthcare System, San Antonio, TX, 9/30/2010

PROFESSIONAL MEMBERSHIPS/ACTIVITIES

Professional Society Activities, with Offices Held National and International

American Association of Cancer Research

Member, 1996-present

Felix Rutledge Society

Member, 1996-present

Chairman, Program Committee, 1999

Co-Chairman, Program Committee, 2007

President, 2008-2009

Society of Gynecologic Oncology

Member, 1996-present

Member, Program Committee, 1999

Member, Government Relations Committee, 2002-2011

Co-Chair, Government Relations Committee, 2005-2011

American Society of Clinical Oncology

Member, 1997-present

American College of Obstetrics and Gynecology

Fellow, 1999-present

Gynecologic Oncology Group

Member, Developmental Therapeutics Committee, 2001-2011

Member, Phase I Subcommittee, 2004-2011

NEOMED Alumni Board

Rootstown, OH

Member 2008-present

Southern Regional Professional Development Conference for Women in Medicine and Research, Take charge of Your Life: Speak Up, Stand Out, and Stay Calm

Member, Planning Committee, 3/2007

American Gynecological & Obstetrical Society

Fellow, 11/2007-present

Southwest Oncology Group (SWOG), Seattle, WA

Member, 11/2010-2011

Local/State

Houston Gynecology & Obstetrics Society, Houston, TX

Member, 1996

Treasurer, 1998-2000

Vice President, 2001-2002

President-Elect, 2002-2003

President, 2003-2004

Member, 2004-2011

Ob-Gyn Alumni Association, The University of Texas Health Science Center at San Antonio, San Antonio, TX

Member, 1999

American Board of Obstetrics & Gynecology, Dallas, TX

Oral Board Examiner, 12/2008

Oral Examiner, 12/2009

Examiner, 12/2010

MEDIA: LOCAL AND NATIONAL

1. News Article on Women's Health On Alert Conference: Wiley, Miryam (Townsmen Correspondent)
Women and hormonal health - the expert views. The Wellesley Townsman: townonline.com, April 7, 2005
2. Lecturer, Breaking the Silence on Ovarian Cancer - Diagnosis and Treatment; NOCC, State of

Disease, Teleconference in Advance of Nation's Leading Cancer Meeting, Taped in New York, NY,
Televised Live Across the Nation, May 22-23, 2006

3. Lecturer, Breaking the Silence on Ovarian Cancer - Diagnosis and Treatment; NOCC Media Initiative Magazine Interview, Interviewed in New York, NY, Fitness, MEDIZine's Healthy Living, Family Circle, Prevention, Cosmopolitan, Glamour, Woman's Day, O Magazine, March 11-13, 2007
4. Lecturer, Breaking the Silence on Ovarian Cancer Campaign, NOCC Media Alert Blitz on the Consensus of Ovarian Cancer; Teleconference in Advance of Nation's Leading Cancer Meeting, Taped in Houston, Texas, Televised Live Across the Nation, June 25, 2007
5. Dr. Oz Show appearance, Birth Control Pills and Risk of Ovarian Cancer, March 2012
6. I Heart Radio, "Preview of Highlights of San Antonio Breast Cancer Society Meeting", December 2013

COMMUNITY

1. Founder, Sprint for Life Fun Run, Raised Well Over \$3.6 Million to Date For Cancer Research, 1998-Present
2. Foundation Event – Development Reception for Banner MD Anderson Cancer Center, November 3, 2011
3. Foundation Event – Presentation at Vi Community, Scottsdale, Arizona 02/2012
4. Banner Health Foundation Lunch - JoAnn Orefice, Pat McKennon and Pat Carbone Tour and Lunch, March 30, 2012
5. Foundation Event – Freeport McMoRan Employee Campaign Launch, Phoenix, AZ , April 6, 2012
6. Surgery Grand Rounds, Banner Good Samaritan Hospital, Gynecologic Oncology 2012 Updates, Phoenix, AZ, March 2012
7. Foundation Event – Bill and Anne Smith Reception, Sedona, AZ April 21, 2012
8. Foundation Event – Presentation at Vi Community, Scottsdale, Arizona 09/12/2012
9. Speaker at 4th Annual Run/Walk for Ovarian Cancer, Break the Silence, NOCC 09/23/2012
10. Speaker at Association of Physician Assistants in Oncology, 2012 Annual Conference, Scottsdale, AZ 10/13/2012
11. Obesity and Cancer, Banner Gateway Medical Center Bariatric Grand Rounds, 02/2013
12. Advanced Leadership Program for Physicians, Banner Health, 2012-2013
13. Principal-Investigator, Various Donors, UT M. D. Anderson Cancer Center, 1999-Present, \$324,834
14. Selected 2013 *Top 50 Most Influential Women in Business*

NATIONAL PROFESSIONAL LECTURES/TALKS

Lecturer: **Strengthening Her Fight in the Battle Against Ovarian Cancer; Physicians Connect-Tibotec (Doxil) Pharmaceuticals & MediMedia**

Houston, TX, October 11, 2005
Woodlands, TX October 12, 2005
Moline, IL, October 25, 2005
Monrovia, CA, October 27, 2005
Grand Rapids, MI, December 15, 2005
Kansas City, MO, January 10, 2006
Houston, TX, October 17, 2006
Oklahoma City, OK, November 14, 2006
Woodlands, TX, April 23, 2007
Oklahoma City, OK, May 8, 2007
Houston, TX, June 12, 2007
Houston, TX, June 19, 2007
Houston, TX (MDACC), June 22, 2007
Houston, TX, October 17, 2007
Houston, TX, December 5, 2007
Houston, TX, June 6, 2008
Houston, TX, May 14, 2009

Lecturer: **Latest Developments in HPV-Related Diseases and Cervical Cancer; Merck i-Med Conference**

Lubbock, TX, September 26, 2006
Dallas, TX, October 10, 2006
Tyler, TX, October 24, 2006
Harvey, LA, November 16, 2006
Beaumont, TX, November 20, 2006
Snyder, TX, November 21, 2006
Bedford, TX, January 18, 2007
Denver, CO, January 30, 2007
Houston, TX, February 13, 2007
Baytown, TX, February 20, 2007
Houston, TX, March 14, 2007
Austin, TX, March 28, 2007
Arlington, TX, May 14, 2007
Houston, TX (MDACC), May 18, 2007

Webster, TX, May 23, 2007
Woodlands, TX, June 7, 2007
Dallas, TX, June 8, 2007
Chicago, IL, July 23, 2007
Nacogdoches, TX, October 30, 2007
Houston, TX, November 11, 2007
San Antonio, TX, November 14, 2007
Dallas, TX, December 4, 2007
Dallas, TX, December 14, 2007
Grapevine, TX, February 4, 2008
San Antonio, TX, February 18, 2008
San Angelo, TX, February 19, 2008
Nacogdoches, TX, February 28, 2008
Hutchinson, KS, May 12, 2008

Lecturer: **The Management of Cervical Cancer: Focus on Hycamtin; Advanced Communication and Education (ACE) - Glaxo Smith Klein (GSK)**

Beaumont, TX, October 30, 2006
Corpus Christi, TX, November 27, 2006
Lafayette, LA, November 28, 2006
Lake Charles, LA, April 2, 2007

Grand Rounds Speaker: **Comprehensive Management of Ovarian Cancer: Current Treatment and Maximizing Quality of Life; Medical Communications Media Bureau**

Casper, WY, September 11, 2007
Pensacola, FL, October 9, 2007
Sugarland, TX, November 9, 2007
Houston, TX, December 4, 2007
Victoria, TX, December 5, 2007
Birmingham, AL, April 1, 2008
Kansas City, MO, May 7, 2008
St. Petersburg, FL, August 21, 2008
Victoria, TX, December 3, 2008
Newport Beach, CA, December 4, 2008

Lecturer: **The Treatment of Platinum-Sensitive Advanced Ovarian Cancer; Lilly Lecturer Bureau**

Houston, TX, April 3, 2007
Harlingen, TX, 12pm & 7pm, Jan 31, 2008
McAllen, TX, March 26, 2008
Brownsville, TX, March 26, 2008
Jacksonville, FL, April 23, 2008
Houston, TX, May 5-6, 2008
Fort Worth, TX, May 14, 2008
Wichita Falls, TX, May 14, 2008
Houston, TX, May 15, 2008
San Antonio, TX, May 28, 2008
Houston, TX, June 4, 2008
San Antonio, TX, July 2, 2008
Beaumont, TX, July 23, 2008
Fort Worth, TX, August 27, 2008
Wichita Falls, TX, August 27, 2008
Indianapolis, IN, (3-ta ks), September 3, 2008

Corpus Christi, TX, September 17, 2008

Laredo, TX, September 17, 2008

San Antonio, TX, October, 22, 2008

Temple, TX, May 22, 2009

Laredo, TX, May 27, 2009

McAllen, TX, May 28, 2009

Houston, TX, June 4, 2009

Houston, TX, June 17, 2009

Beaumont, TX, August 6, 2009

CV updated; 09/24/2014

Judith K Wolf, MD

Updated 7/6/2016

Exhibit B

- “A Survey of the Long-Term Effects of Talc and Kaolin Pleurodesis.” *British Journal of Diseases of the Chest* 73 (1979): 285–88. [https://doi.org/10.1016/0007-0971\(79\)90054-8](https://doi.org/10.1016/0007-0971(79)90054-8).
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Exhibit 4

**UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY**

**IN RE JOHNSON & JOHNSON
TALCUM POWDER PRODUCTS
MARKETING, SALES PRACTICES,
AND PRODUCTS LIABILITY
LITIGATION**

MDL NO. 16-2738 (FLW) (LHG)

THIS DOCUMENT RELATES TO ALL CASES

**RULE 26 EXPERT REPORT OF
ELLEN BLAIR SMITH, MD**

Date: November 16, 2018



Ellen Blair Smith, MD

As a physician who specializes in the treatment of women with cancer (including ovarian cancer), I was asked to provide professional opinions on the question of whether the genital use of talcum powder products can cause ovarian cancer. I was also asked, if I found this to be the case, to further provide opinions on the biological mechanism(s) for this effect.

BACKGROUND AND QUALIFICATIONS

My name is Ellen Blair Smith. My attached CV reports my education and medical training. I practiced gynecologic oncology in Charlottesville, Virginia from July 1984 until February 1987 as an assistant professor at the University of Virginia. I then left academic medicine to open my own private practice of gynecologic oncology in Austin, Texas. That practice involved care of women known or suspected to have gynecologic cancers and continued for more than 28 years. During these years, I was responsible for all aspects of the care of hundreds of women with epithelial ovarian cancer. That care involved diagnosis, preoperative, surgical, and postoperative care, chemotherapy selection and administration and post-treatment care and surveillance. All too often post-treatment surveillance led to the diagnosis of recurrent cancer and the treatment cycle resumed. All too often, after months or years (up to 21 years of care for one patient), I provided end-of-life care for my patients.

My dissatisfaction with the inadequacies of screening systems to detect ovarian cancer early led me to follow enthusiastically the discoveries of genes that increase the risk of ovarian cancer and to aggressively promote the detection of such genes. Before these tests were commercially available, I worked with geneticist-physicians at the University of Pennsylvania and Duke University to detect these genes in my patients with ovarian cancer and their daughters. I was an early advocate of risk-reducing salpingo-oophorectomy and lectured throughout Texas by invitation of the Texas Medical Association. In 2004, Myriad Genetics (which had patented the BRCA test) asked me to be its first gynecologic oncologist speaker. Until roughly 2011, I delivered many lectures to gynecologic colleagues throughout the US.

In November 2001, I took a leave of absence and moved to Paris, France, with my children while my husband pursued a Guggenheim fellowship there. While there, I returned to the US to attend the Society of Gynecologic Oncologists to hear the latest research in ovarian cancer presented. I also attended a European Cancer conference in Paris and was excited to first hear the results of the Scottish Randomised Trial in Ovarian Cancer (SCOTROC), a large international randomized trial comparing two different chemotherapy regimens for the treatment of epithelial ovarian cancer ovarian cancer trial in which I enrolled patients. I returned to my practice in August of 2002.

To enhance the end of life care of my gynecologic oncology patients, I pursued further education in Hospice and Palliative Care, passing the written examination to become board certified in 2010. I retired from my gynecologic oncology practice in December of 2015. In April of 2017, I returned to patient care as medical director of Halcyon Home Hospice. In my role with a hospice organization, I continue to care for patients with ovarian and other cancers. My CV is attached as Exhibit A.

METHODOLOGY

In preparing this report, I began with a comprehensive review of the medical literature. I relied on PubMed searches on many topics, including talc and ovarian cancer, as well as searched authors. I then read many of the references of the articles cited in those papers. I sometimes followed this research with searches on Google or Google Scholar on the same subjects to assure that I had found all relevant references. This literature included epidemiological studies, review articles, mechanistic articles and opinion articles on this topic and related subjects. I additionally reviewed information, including Johnson & Johnson and Imerys company documents that I either requested or considered relevant to my opinions. These were provided by plaintiffs' attorneys. Finally, I drew on my own educational resources, as well as my education, training, and experience caring for patients with ovarian cancer. This is the same methodology and scientific rigor that I have used regularly in my professional career and clinical practice, to explore and understand a topic of interest.

OVERVIEW OF OVARIAN CANCER

Cancers of the ovary may arise from the epithelium/mesothelium covering the ovary, called epithelial ovarian cancer (EOC); from the oocytes of the ovary, called germ cell tumors; or, more rarely, from the hormone-producing cells of the ovary, the sex cord-stromal tumors. This report addresses EOC, the type of ovarian cancer associated with talcum powder exposure.

Pathogenesis

The history as to the origin of ovarian cancer must be divided into before 2008 and after 2008. Before 2008, incessant ovulation and the repair of the monthly breaks in ovarian surface epithelium was believed to be responsible for EOC. (Fathalla 1971). That more DNA errors would be generated with more ovulation defects made intuitive sense and seemed to be supported by the epidemiologic evidence of higher parity (ovulation free windows) decreasing risk of EOC (La Vecchia 2017). Furthermore, the first generation of high estrogen oral contraceptives that blocked ovulation also decreased ovarian cancer. (Havrilesky et al. 2013) Levanon proposed that EOC is, in fact, two different diseases with two etiologies; the premalignant state of Type II was, as yet, unidentified. Budding molecular data support this division. (Levanon, Crum, and Drapkin 2008).

Until 2008, EOC was thought distinct from fallopian tube cancer and primary peritoneal cancer. While the cell of origin for all these cancers appears similar, many papers were published and conventions defined to separate them. The pioneering work of scientists/physicians at Brigham and Women's and the Dana Farber revealed that many EOCs arise in the fallopian tube and metastasize to the ovary and/or peritoneum, at least in women who harbor genetic homologous repair defects. (Levanon, Crum, and Drapkin 2008). Both Fathalla and the researchers at Brigham and Women's have updated and more clearly defined their hypotheses in light of the increased role of fallopian tube epithelium in EOC and growing molecular data. (Levanon, Crum, and Drapkin 2008; Fathalla 2013). Dubeau and Drapkin include and support the role of extrauterine Mullerian epithelium, as well as tubal and ovarian epithelium, in their hypotheses of pathogenesis of EOC. (Dubeau and Drapkin 2013). For our purposes, we consider epithelial

cancers of the ovary, fallopian tubes, and peritoneum to be a single entity. All are associated with talcum powder usage

The quest for a molecular understanding of the ways EOC arise is ongoing, but has also been described extensively. There are certain factors that can initiate the cascade of DNA changes that cause unregulated proliferation, acquisition of more DNA damage, and inhibition of programmed cell death (apoptosis) - the normal fate of abnormal cells in a healthy system. For example, loss of TP53 (a gene essential for regulating cell division and preventing tumor formation), function has been shown to appear early in the genesis of serous EOC. (Chien et al. 2015).

Risk Factors

Generally accepted risk factors for EOC, in addition to talcum powder and asbestos, include inherited gene mutations, family history, obesity, nulliparity, advanced age, history of endometriosis, infertility, polycystic ovarian syndrome, intrauterine devices, pelvic inflammatory disease, early menarche and late menopause. Additionally, there are factors that are recognized as protective. These include tubal ligation/sterilization (TS), oral contraceptive use, salpingectomy, salpingo-oophorectomy, hysterectomy, and breast feeding. (Hunn and Rodriguez 2012; Mallen, Townsend, and Tworoger 2018; Park et al. 2018; Folkins et al. 2018). Risk factors are not mutually exclusive. They can be cumulative, additive, and synergistic. (Vitonis, Titus-Ernstoff, and Cramer 2011; S. Wu et al. 2018).

Inherited gene mutations, such as BRCA-Fanconi anemia pathway and Lynch syndrome mismatch repair genes, are discussed in another section.

The Ovarian Cohort Consortium pooled data from 21 prospective cohort studies on 1.3 million women. (Wentzensen et al. 2016). In these studies, 5584 women were diagnosed with EOC and risk comparisons were made for parity, oral contraception use, breast feeding, age at menarche, age at menopause, menopausal HRT use, tubal ligation, endometriosis, first degree family history of breast cancer, first degree history of ovarian cancer, BMI, height, and smoking). In a group this large, histologic subclassification could be done and associations were made for serous/poorly differentiated EOC, endometrioid EOC, clear cell EOC and mucinous EOC. One thousand EOC patients had “other” or missing histologic information. Multiparity decreased risk in all ovarian cancer subtypes. Oral contraceptive use for 5 years and for 10 years decreased risk in all but mucinous tumors. Late menopause increased risk in only endometrioid and clear cell cancers.

Diagnosis

The diagnosis of EOC may occur at surgery for a pelvic mass, incidentally at surgery for another reason, or by cytologic evaluation of paracentesis of ascites.

Staging

Ovarian cancer, regardless of cell type, is staged surgically. By convention, we use International Federation of Gynecology and Obstetrics (FIGO) staging. The staging system changes every 10-

15 years as data allowing discrimination are reviewed. It was always my practice to note in a patient's chart the original stage and year of that staging versus contemporary stage.

STAGE I: Tumor confined to ovaries					
OLD			NEW		
IA	Tumor limited to 1 ovary, capsule intact, no tumor on surface, negative washings/ascites.		IA	Tumor limited to 1 ovary, capsule intact, no tumor on surface, negative washings.	
IB	Tumor involves both ovaries otherwise like IA.		IB	Tumor involves both ovaries otherwise like IA.	
IC	Tumor involves 1 or both ovaries with any of the following: capsule rupture, tumor on surface, positive washings/ascites.		IC Tumor limited to 1 or both ovaries		
			IC1	Surgical spill	
			IC2	Capsule rupture before surgery or tumor on ovarian surface.	
			IC3	Malignant cells in the ascites or peritoneal washings.	

STAGE II: Tumor involves 1 or both ovaries with pelvic extension (below the pelvic brim) or primary peritoneal cancer					
OLD			NEW		
IIA	Extension and/or implant on uterus and/or Fallopian tubes		IIA	Extension and/or implant on uterus and/or Fallopian tubes	
IIB	Extension to other pelvic intraperitoneal tissues		IIB	Extension to other pelvic intraperitoneal tissues	
IIC	IIA or IIB with positive washings/ascites.				

****Old stage IIC has been eliminated****

STAGE III: Tumor involves 1 or both ovaries with cytologically or histologically confirmed spread to the peritoneum outside the pelvis and/or metastasis to the retroperitoneal lymph nodes				
OLD			NEW	
IIIA	Microscopic metastasis beyond the pelvis.		<i>IIIA (Positive retroperitoneal lymph nodes and /or microscopic metastasis beyond the pelvis)</i>	
			IIIA1	<i>Positive retroperitoneal lymph nodes only</i>
				<i>IIIA1(i) Metastasis ≤ 10 mm</i>
				<i>IIIA1(ii) Metastasis > 10 mm</i>
			IIIA2	<i>Microscopic, extrapelvic (above the brim) peritoneal involvement ± positive retroperitoneal lymph nodes</i>
IIIB	Macroscopic, extrapelvic, peritoneal metastasis ≤ 2 cm in greatest dimension.		IIIB	<i>Macroscopic, extrapelvic, peritoneal metastasis ≤ 2 cm ± positive retroperitoneal lymph nodes. Includes extension to capsule of liver/spleen.</i>
IIIC	Macroscopic, extrapelvic, peritoneal metastasis > 2 cm in greatest dimension and/or regional lymph node metastasis.		IIIC	<i>Macroscopic, extrapelvic, peritoneal metastasis > 2 cm ± positive retroperitoneal lymph nodes. Includes extension to capsule of liver/spleen.</i>

STAGE IV: Distant metastasis excluding peritoneal metastasis				
OLD			NEW	
IV	Distant metastasis excluding peritoneal metastasis. Includes hepatic parenchymal metastasis.		IVA	<i>Pleural effusion with positive cytology</i>
			IVB	<i>Hepatic and/or splenic parenchymal metastasis, metastasis to extra-abdominal organs (including inguinal lymph nodes and lymph nodes outside of the abdominal cavity)</i>

FIGO Ovarian Cancer Staging Effective Jan. 1, 2014.¹

Treatment

The treatment of ovarian cancer is usually straight-forward: surgically remove all the visible cancer, establish locations of invisible cancer (microscopic metastases, define best treatment and prognosis, then treat -in the majority of cases - with a taxane and a platinum chemotherapy doublet. (Vasey et al. 2004; Armstrong et al. 2006).

However, seventy-five percent of ovarian cancer cases present with metastases to the upper abdomen or beyond. Suboptimal debulking (leaving grossly visible tumor) has no survival benefit over primary chemotherapy. (Horowitz et al. 2015). The physicians at MD Anderson established a protocol for preoperative laparoscopy and the opinions of two trained gynecologic oncologists, in concert with clinical and laboratory findings, to judge whether a tumor was resectable. (Nick et al. 2015). These “debulking” surgeries are quite complex, require specialized training, and often necessitate consultation from other surgical specialties.

¹ https://www.sgo.org/wp-content/uploads/2012/09/FIGO-Ovarian-Cancer-Staging_1.10.14.pdf

Chemotherapy with a platinum and a taxane follows. These drugs may be delivered intravenously or intraperitoneally. Usually, six cycles of chemotherapy are given. Remission occurs in over 70% of patients, as evidenced by CT scans, physical examination, and CA125 (a clinically used biomarker for screening and detection) levels. Surveillance begins.

In patients with Stage III and IV (typically 75% of patients with EOC), recurrence will follow in 5-24 months. Then we evaluate again for surgery (isolated focal recurrence versus multifocal or unresectable recurrence) and additional chemotherapy. (Rasool et al. 2010; Parmar et al. 2003).

This cycle typically continues until my patient's tumor has become resistant to platinum and two other agents. At that time, the probability of her tumor responding to any standard chemotherapy is essentially nonexistent. We discuss clinical trials and/or end-of-life care. Regardless of her treatment choices, she dies in 6-12 months. Her death is protracted, usually from starvation, due to multiple bowel obstructions. Ideally, pain is controlled.

5 Year Survival Rates

The following are 5-year survival rates according to the American Cancer Society Website. As the new FIGO staging just started in 2014, 5-year data is not yet available.

I 78%

IA 93%

IB 91%

IC 84%

II 61%

IIA 82%

IIB 72%

IIC 67%

III 28%

IIIA 63%

IIIB 53%

IIIC 41%

IV 19%.²

Modern surgery and chemotherapy have changed the natural history of ovarian cancer. Late recurrence (after 5-year) is common. Ten-year survival does not mean cure. I have personally treated late recurrences after ten years of remission. Others have reported these findings as well. (Baldwin et al. 2012; Tewari et al. 2015)

² <https://www.cancer.org/cancer/ovarian-cancer/detection-diagnosis-staging/survival-rates.html>

OVARIAN CANCER GENETICS

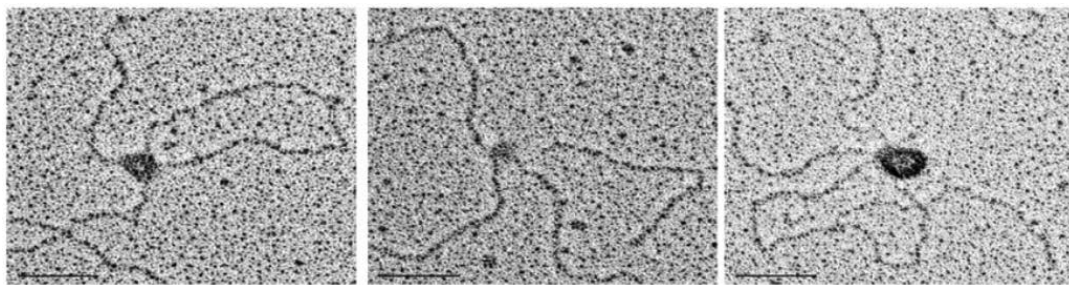
All cancer is genetic; that is, cancer involves DNA changes occurring in the chromosomes of a cell that was initially normal. For epithelial cancers, this is usually a series of mutations, DNA breaks, alterations (such as methylation), deletions, rearrangements or DNA amplification. These changes do not necessarily progress linearly. Watson reviewed some of these complexities in a recent article in *Nature*. (Watson et al. 2013).

A Cancer Genome Atlas Research Network (TCGA) study published in 2011 analyzed 489 high grade serous ovarian cancers (HGSOC). Exon sequencing of 316 of these tumors was performed. It identified the nearly universal (96%) presence of somatic mutations in the gene TP53 in HGSOC. That mutation seems to be a first step towards the development of EOC. Ovarian cancers occur in <3% of women with germline, heritable TP53 mutations; breast cancer is much more frequently occurring. (K. D. Gonzalez et al. 2009). Genes in homologous repair pathway were mutated in 49% (with better prognosis for those with germline mutations as opposed to somatic mutation or methylation). The FOXM1 transcription factor network was activated in 87%. This family of genes is involved in regulating cell cycle and differential gene expression. (Hannenhalli and Kaestner 2009; X. Chen et al. 2013).

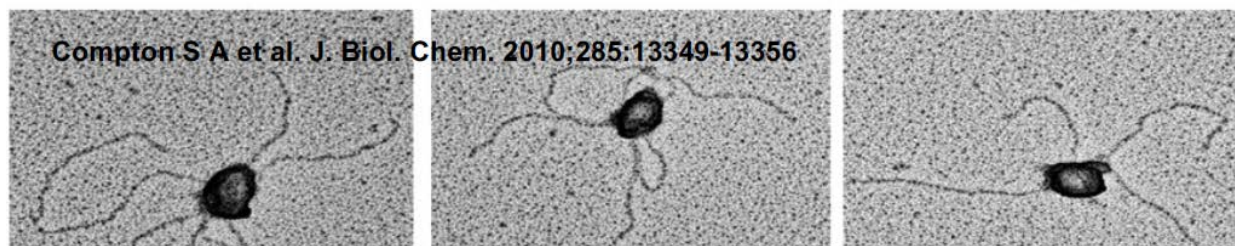
Interest in the homologous repair pathway has exploded since Mary Claire King's identification of what we now know to be the tumor suppressor gene, BRCA1. (Hall et al. 1990).

Homologous DNA repair is double stranded DNA repair breaks. This pathway includes multiple genes including BRCA1, BRCA2, Rad 51B, Rad 51C, Rad 51D, BRIP1, PALB2 and others. The protein products of this family of multiple genes work together to repair DNA. (Compton, Ozgür, and Griffith 2010; Thai et al. 1998). Binding of BCDX2 or CX3 to Holliday Junction DNA CX3 (A) or BCDX2 (B) was incubated with Holliday junction templates, mounted onto carbon-coated copper grids, and rotary shadowcast with tungsten for visualization by EM. Images are shown in reverse contrast. (Compton, Ozgür, and Griffith 2010).

A



B



The ring structure in A is a complex of Rad 51C and Xrcc3. The ring structure in B is a complex of Rad 51B, Rad 51C, Rad 51D and Xrcc2.

Germline deficiencies in any of these genes have been shown to result in an increased risk of EOC. Why? Knudson answered that in simple terms (Knudson 1971). To be born deficient in one half of a DNA repair enzyme is to be born one step closer to cancer; target cancers appear earlier and more frequently. Many early studies note the increased incidence of breast cancer with BRCA1 and BRCA2 germline mutations carriers: over 80% by age 70. (Ford et al. 1998). They also give the increased risks of ovarian cancer: for BRCA1, 39% by age 70, and for BRCA2, 11% by age 70 studied 1915 patients with ovarian cancer and detected germline mutations in BRCA1 and BRCA2, RAD51B, Rad51D, PALB2, BARD1, BRIP1 (the HR repair pathway), as well as the genes involved in Lynch Syndrome. (Antoniou et al. 2003; Norquist et al. 2016).

Penetrance is the phenotypic expression of underlying genetic aberrations. Why does one woman with a BRCA1 mutation exhibit breast and/or ovarian cancer while another woman with the SAME mutation does not? Penetrance is influenced by environmental and genetic factors. For example, epidemiologic studies have shown that breast feeding and tamoxifen use decrease the risk of manifesting breast cancer in carriers of BRCA1 mutations. (Friebel, Domchek, and Rebbeck 2014). This same review and meta-analysis shows that oral contraceptives use decreases risk for ovarian cancer in BRCA1 and BRCA2 mutation carriers. Other known risk factors can interact with individuals who have an inherited gene mutation to increase the risk. In other words, women with BRCA and other hereditary gene mutations, are at least as susceptible to other reproductive, environmental, or inflammatory risk factors as women who do not have mutations. This would be expected with BRCA mutation carriers exposed to talcum powder products.

Factors that decrease penetrance may be external or environmental factors, as mentioned above, or may be intrinsic factors, genetic, or epigenetic. Rebbeck et al. demonstrated that the location of the mutation in these huge BRCA genes is a determinant of risk of manifestation of breast and/or ovarian cancer. (Rebbeck et al. 2015). Genetic and epigenetic modifiers became the focus of the CIMBA (Consortium of Investigators of Modifiers of BRCA1/2). (CIMBA et al. 2007). This international consortium of sixty groups of researchers are identifying genetic modifiers to BRCA breast and ovarian cancer risks as single nucleotide polymorphisms (SNPs) in nonBRCA genes. (Ding et al. 2012; Ramus et al. 2012). Such SNPs modify penetrance. Epigenetic changes such as methylation in promoter regions of genes also affect risk of ovarian cancer development.

EPIDEMIOLOGICAL STUDIES

The first epidemiological study was published in 1982 by Cramer, et al, Cancer (1982) 50:372 “Ovarian Cancer and Talc: A Case-Control Study.” (D. W. Cramer et al. 1982). Since that time, there have been numerous additional epidemiological studies.

The Meta-analyses and Pooled Study

Harlow et al, 1992:

This study (of which Cramer is a coauthor) offers the first meta-analysis of the perineal talcum powder use and risk of ovarian cancer in their case-control study of 235 Boston-area women hospitalized in ten area hospitals. Controls were selected from the population and generated from “townbooks” by random number generation selecting the book page and age matched. “Ever” perineal talcum powder use vs none generated a OR of 1.5 (95% CI 1.0-2.1). The meta-analysis follows:

Table 6. Odds Ratios With 95% Confidence Intervals of Ovarian Cancer in Relation to Any Perineal Exposure to Talc as Reported in Previous Epidemiologic Studies

Author(s) (year)	Cases		Controls		Crude OR	95% CI
	Total	Talc exposure	Total	Talc exposure		
Cramer et al ⁴ (1982)	215	92 (42.8%)	215	61 (28.4%)	1.9	1.3–2.9
Hartge et al (1983)*	135	67 (49.6%)	171	100 (58.5%)	0.7	0.4–1.1
Whittemore et al ⁵ (1988)	188	98 (52.1%)	539	248 (46.0%)	1.4	0.9–2.0
Harlow and Weiss ⁶ (1989) [†]	116	49 (42.2%)	158	64 (40.5%)	1.1	0.7–2.1
Booth et al ⁷ (1989)	217	141 (65.0%)	434	256 (59.0%)	1.3	0.9–1.9
Harlow et al (1992) (current study)	235	114 (48.5%)	239	94 (39.3%)	1.5	0.9–1.8
All studies [‡]	1106	561 (50.7%)	1756	823 (46.9%)	1.3	1.1–1.6

The authors conclude that “there is an association, albeit modest, between ovarian cancer and peritoneal talc use” They state that this association may be due to asbestos contamination in talcum powder produced before 1976. This study was supported by an NCI grant. (Harlow et al. 1992).

Gross and Berg, 1995

These investigators analyzed 9 case-control studies (D. W. Cramer et al. 1982; Hartge et al. 1983; Whittemore et al. 1988; Booth, Beral, and Smith 1989; Harlow and Weiss 1989; Y. Chen et al. 1992; Harlow et al. 1992; Rosenblatt, Szklo, and Rosenshein 1992; Tzonou et al. 1993) and combined those studies with preliminary (and mathematically manipulated) data from Hankinson et al’s 1993 report on the Nurses’ Health Study. The Nurses’ Health Study was not completed until 1996; talc use was not queried in the first 8 years of the study. By Gross’ and Berg’s estimate the RR of “ever genital talc use” vs “never” use is 0.6 (95% CI 0.38-1.02). In fact, that is a low RR as the Nurses’ study showed and overall RR of ever vs never use and epithelial ovarian cancer of 1.09 (95% CI 0.86-1.37). (Gertig et al. 2000, see below).

192 *Gross and Berg***TABLE 3. Results of the Meta-Analyses**

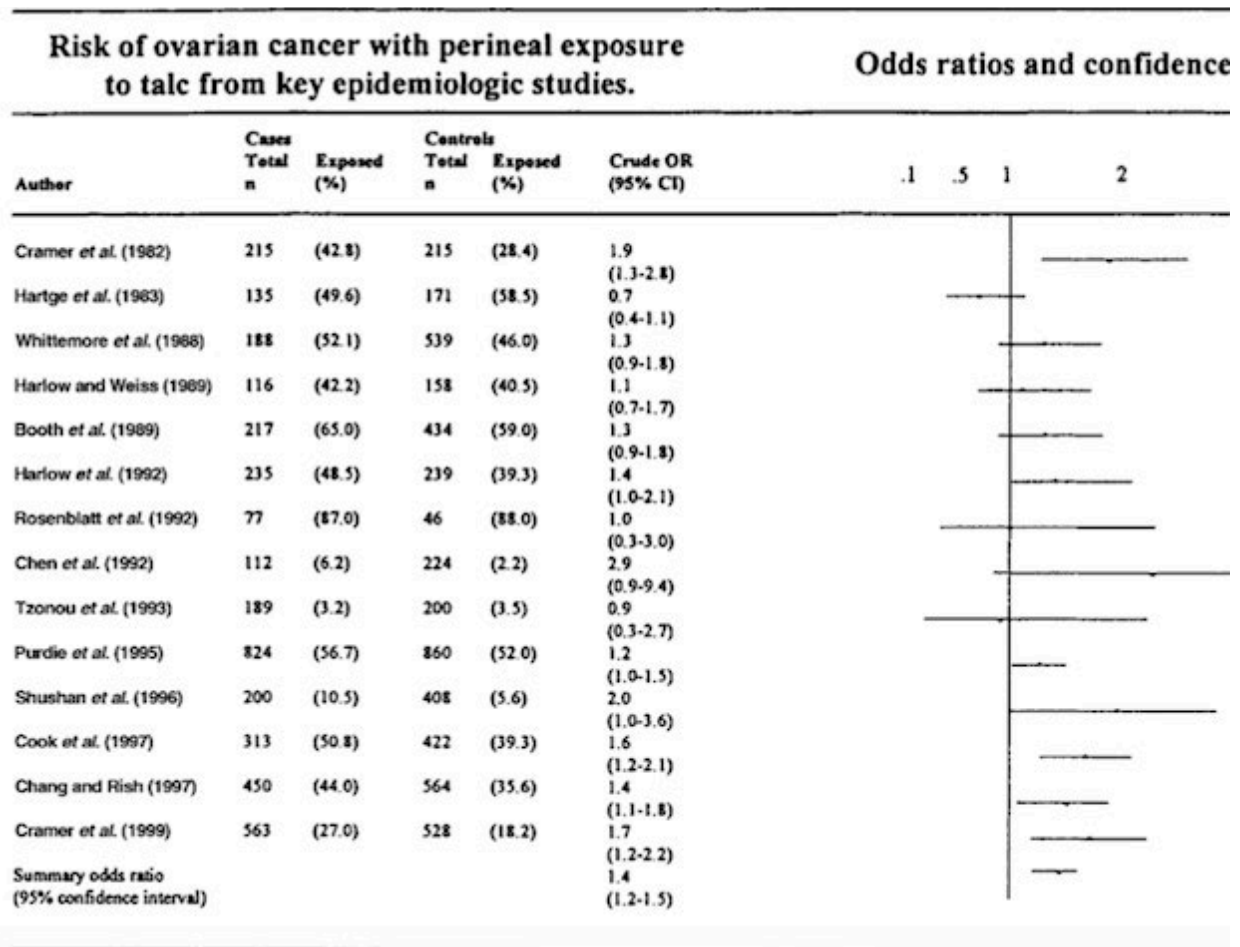
Analysis	Studies used	<i>Q</i> (degrees of freedom)	RR (95% CI)
Crude risk, both tumor types	All	11.884 (8)	1.27 (1.09–1.48)
Adjusted risk, both tumor types	CRAM, HART, WHIT, HAR1, HAR2, CHEN, and TZON	9.043 (6)	1.31 (1.08–1.58)
Crude risk, epithelial tumors	HART, WHIT, BOOT, HAR2, ROSE, CHEN, and TZON	7.19 (6)	1.20 (1.01–1.44)
Adjusted risk, epithelial tumors	HART, WHIT, HAR2, CHEN, and TZON	7.598 (4)	1.29 (1.02–1.63)

The authors demonstrated that “all meta-analyses arrive at relative risks greater than 1.0 with 95% confidence intervals excluding the null.” Despite these findings, the authors conclude that “existing evidence linking talc exposure to an increased risk of ovarian cancer cannot be viewed as scientifically conclusive”. A dose response relationship is not demonstrated. This study was supported by Johnson and Johnson. (Gross and Berg 1995).

Cramer et al, 1999

In 1999, Cramer et al (with Harlow as a coauthor) published a new case-control study of 563 epithelial ovarian cancers, including 86 serous borderline tumors. Controls were 523 women. No increased risk of ovarian cancer was seen in never users of powder vs non-genital powder users. For those who never used or had nongenital powder use vs any genital use, the odds ratio was 1.60 (95% CI 1.18-2.15) for development of ovarian cancer. Adjustments for age, community, parity, oral contraceptive use, BMI, and family history of breast or ovarian cancer were made.

These authors then did meta-analysis with the following results:



Cramer *et al.* conclude that “a consistent association between talc and ovarian cancer appears unlikely to be explained by recall bias or confounding” (page 356). This study, too, was supported by a grant from the National Cancer Institute. (Cramer 1999).

Huncharek *et al.*, 2003

Sixteen case control studies (Booth, Beral, and Smith 1989; C.-J. Chang *et al.* 2017; Y. Chen *et al.* 1992; Cook, Kamb, and Weiss 1997; D. W. Cramer *et al.* 1982; D. W. Cramer 1999; Godard *et al.* 1998; Harlow and Weiss 1989; Ness *et al.* 2000; Purdie *et al.* 1995; Rosenblatt, Szklo, and Roshenhein 1992; Tzonou *et al.* 1993; Whittemore *et al.* 1988; Wong 1999) were found to be homogeneous and delivered 11,933 subjects (4959 cases). Pooled meta-analysis of ever perineal talcum powder use versus no exposure “yielded a summary relative risk of 1.33 with a 95% confidence interval of 1.16-1.45, a statistically significant result suggesting a 33% increased risk of developing ovarian cancer”. No dose response was found. However, the study did not collect the necessary data to permit this determination. Huncharek *et al.* spend the rest of the paper dismissing their result as NOT supporting an association between talc and ovarian cancer. According to the disclosure, this research was partially supported by the Marshfield Medical Research Foundation. There was no mention of financial support from Johnson & Johnson or Imerys (although disclosed in a 2007 paper by the same authors – Huncharek 2007).

Langseth et al 2008

The Langseth study drew data from The International Agency on Cancer Research (IARC) review of the literature, published as a Monograph in 2010 (which classified non-asbestiform talc as possibly carcinogenic)³, but did not provide a comprehensive report on this review or the findings. IARC was founded in 1965 and comprises investigators from 25 countries who “promote international collaboration in cancer research” (IARC.fr website). Langseth found an OR of 1.35 (95% CI 1.26-1.46), suggesting a statistically significant increase in ovarian cancer risk and concluded that “epidemiological evidence suggests that the use of cosmetic talc in the perineal area may be associated with ovarian cancer risk. Langseth commented in the high degree of consistency in the studies reviewed and proposed that “the mechanism of carcinogenicity may be related to inflammation.”

See insert below.

³ IARC defines Group 2B as follows: Group 2B: The agent is possibly carcinogenic to humans. This category is used for agents for which there is limited evidence of carcinogenicity in humans and less than sufficient evidence of carcinogenicity in experimental animals. It may also be used when there is inadequate evidence of carcinogenicity in humans but there is sufficient evidence of carcinogenicity in experimental animals. In some instances, an agent for which there is inadequate evidence of carcinogenicity in humans and less than sufficient evidence of carcinogenicity in experimental animals together with supporting evidence from mechanistic and other relevant data may be placed in this group. An agent may be classified in this category solely on the basis of strong evidence from mechanistic and other relevant data. (IARC 2012).

Langseth et al, 2008

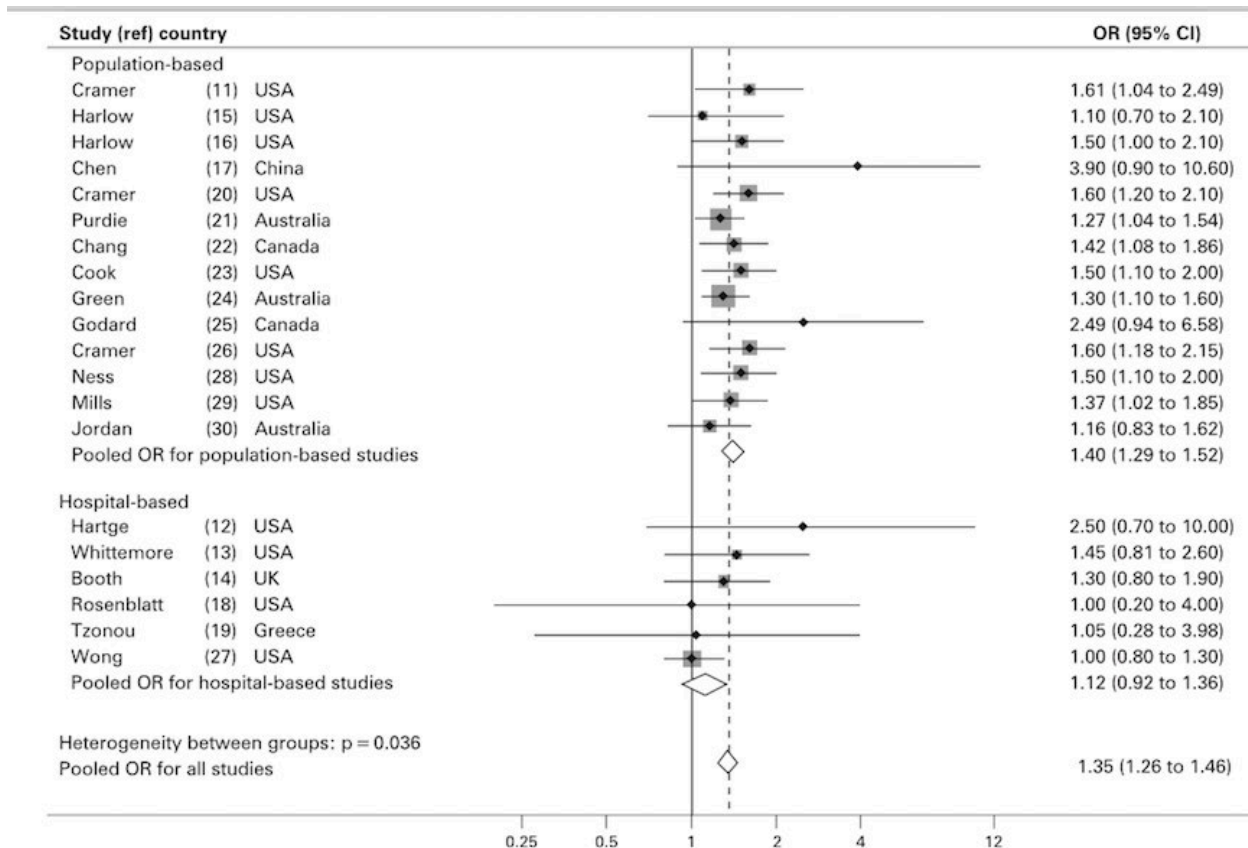


Figure 1 Results from case-control studies contributing data on perineal talc use and ovarian cancer. Results are presented as odds ratios (ORs) and their corresponding confidence intervals (95% CIs) and represented by squares and lines, respectively. Results are separated in 14 population-based and six hospital-based case-control studies. Pooled ORs for all population-based studies combined and all hospital-based studies combined are given OR pooling by fixed effect models (Mantel-Haenszel method).

11=Cramer et al, 1982
 15=Harlow and Weiss, 1989
 16=Harlow et al, 1992
 17=Chen et al, 1992
 20=Cramer and Xu, 1995
 21=Purdie et al, 1995
 22=Chang and Risch, 1997
 23=Cook et al, 1997
 24=Green et al, 1997
 25=Godard et al, 1998
 26=Cramer, 1999
 28=Ness et al, 2000
 29=Mills, et al, 2004
 30=Jordan et al, 2007
 12=Hartge et al, 1983
 13=Whittemore et al, 1988
 14=Booth et al, 1989

19=Tzonou et al, 1993
 27=Wong et al, 1999
 18=Rosenblatt et al, 1992

The Langseth et al study was financed by the Cancer Registry of Norway.

Terry et al, 2013

The Ovarian Cancer Association Consortium, an international, multidisciplinary group, investigates factors related to ovarian cancer development, including case-control studies and identification and analysis of genes associated with cancer risk. It is supported, in part, by the Ovarian Cancer Research Fund, the United States National Cancer Institute, and Cancer Research UK. Raw data from the following studies were pooled and analyzed: Rosenblatt et al, 2011 (including previously unpublished additional patients and data), Goodman et al, 2008 (previous unpublished data on powder use), Lo-Ciganic et al, 2012 (previously unpublished data on powder use), Moorman et al, 2009 (adding previously unpublished patients and data), Cramer et al, 1999 (with additional patient data), Pike et al, 2004 (previously unpublished powder use data), Merritt et al, 2008 (with additional patient data), and Chang et al, 1997 (including previously unreported patient data). Confounders adjusted for include age, oral contraceptive use and duration, parity, tubal ligation, BMI, race/ethnicity. The cases were 8525 cases of ovarian, fallopian tube, and primary peritoneal cancer, reflecting the recognition, in the decade of the 2000s, of the overlap and similarity and possible common etiology of these differently named cancers. In this study, 31% of cases used genital powder, as opposed to 25% of controls. Comparing ever users of genital powder with never users, the OR was 1.24 (95% CI 1.15-1.33). Similar results were seen for genital use vs non-genital use of powder. Risks were stronger for patient with BMI < 30. There was no association with parity, OC use, tubal ligation status, or menopausal status. Histologic break down of the cases showed significant increased risk in both borderline (OR 1.29 [95% CI 1.14-1.48]) and invasive cancers (OR 1.21, [95%CI 1.12-1.32]). Significant increased odds ratios with genital powder use were seen for invasive serous, endometrioid and clear cell tumors, but not invasive mucinous tumors. (Terry et al. 2013).

Penninkilampi and Eslick, 2017

The most recent meta-analysis is from two authors at the University of Sydney in New South Wales, Australia. The authors analyzed 24 case-control studies and 3 cohort studies on perineal talcum powder use and risk of development of ovarian study, excluding studies of fewer than 50 cases and duplicated published data. A total of 14,311 cases of ovarian cancer were included. Quality of the component studies were scored on the Newcastle-Ottawa Scale; none scored perfect, but the lowest score was 5/10, so none were excluded. Long term talcum powder use was judged greater than 10 years and was associated with an increase in ovarian cancer risk of OR=1.25 (95% confidence interval (CI) 1.10-1.43). (Lifetime applications of perineal talc of 3600 times roughly correlates with 10 years use; increased risk of ovarian cancer was found with fewer and more applications than 3600.) "Any perineal talc use was associated with any serous, serous invasive, serous borderline and endometrioid subtypes of ovarian cancer (Figure 2c)." This is the largest meta-analysis to date and continues to support the association of perineal talc use with increasing the risk of epithelial ovarian cancers. (Penninkilampi and Eslick 2018).

The Prospective Cohort Studies

There are three true prospective cohort studies looking at genital talcum powder use to perineum, diaphragms or menstrual pads or such use in some combination.

Gertig 2000

The Nurses' Health Study (Gertig et al, 2000) is a 20-year duration study (1976-1996) of 78,630 nurses age 30-55 (in 1976) in the USA. Perineal talcum powder use was first queried in 1982. The cohort answered questionnaires every other year. Ovarian cancer developed in 307 nurses. The relative risk (RR) for ever use of talcum powder and development of any epithelial ovarian cancer was 1.09 (95% CI 0.86-1.37). Invasive serous ovarian cancer demonstrated a statistically significant elevated multivariate RR of 1.40 (95% CI 1.02-1.9) (controlled for age, parity, duration of oral contraceptive use, BMI, tubal ligation, smoking and menopausal status). No other histologic group (all serous including borderline tumors, endometrioid or mucinous tumors) showed elevated risk with appropriate confidence intervals. Within this study there was no dose-response demonstrated, although P for trend was 0.5. For users over 45 years old in 1982 RR for serous ovarian cancer was 1.51 (95% CI 1.07-2.15). No such increased relative risk for any ovarian cancer type was seen for those under 45 in 1982. Gates (2010) continues the analysis of the NHS, finding no increased risk of any subtype. (Gertig et al. 2000).

Houghton 2014

The Women's Health Initiative Study was published by Houghton et al in 2014. This study of 61,576 postmenopausal women (age 50-79) showed ever-talc-use (perineal, diaphragm, pad) was not associated with statistically significant increased risk of development of any ovarian cancer contrasted to never-use (Hazard ratio=1.12 [95% CI 0.92-1.23]). There were 429 incident cases of ovarian cancer over the 12+ years of this study. In this study, talc use in any form was combined, no histologic information was obtained, and information on frequency of use was not obtained. (Houghton et al. 2014).

Gonzalez 2016

Gonzalez et al, 2016 studied a cohort of sisters or half-sisters of breast cancer patients in the USA. After exclusions, (BSO, missing data), 41,654 women were followed a median of 6.5 years during which 135 ovarian cancer, 5 fallopian tube cancers and 4 peritoneal cancers were diagnosed. Eight other cancers were likely from one of these three sites. (Only 96 cases of cancer were verified by medical record or death certificate review; all other were solely patient-reported at annual questionnaire responses.) At entry, the participants completed questionnaires regarding genital talc use as powders or spray and its frequency and douching. Perineal powder use was inversely associated with the development of ovarian-type cancer (Hazard ratio=0.73 (95% CI 0.42-1.1). Douching during the 12 months prior to study entry was associated with an increased risk of ovarian cancer (HR=1.8 [95% CI 1.2-2.8]), while combined talc and douching in the 12 months antecedent to study entry resulted in an HR=1.8 (95%CI 0.81-3.9). The authors acknowledge that they cannot know which powders contained talc and admit "powder has changed over time..." Additional limitations include small numbers, failure to ask questions about frequency or duration of powder usage, and short-term follow-up. With an expected latency period of over twenty years, this study would not pick up all cases. All of these deficiencies result in a failure to capture the true risk. (Gonzalez et al. 2016).

The Case-Control Studies

Cramer et al.'s landmark 1982 case control study looked at perineal talcum powder use in 215 white patients with epithelial ovarian cancer matched by age, race, and residence to 215

community women. These 215 cases included 39 borderline tumors. All pathology was histologically reviewed. Cases and controls were interviewed as to talc exposure from surgical glove, diaphragm use, and perineal use and/or dusting menstrual pads. Talc use varied between cases (42.8%) and controls (28.4%). Any perineal talc exposure showed an adjusted relative risk of ovarian cancer of 1.92 (95% confidence limits 1.27-2.89). (This relative risk was adjusted for parity and menopausal status.)

In the ensuing thirty-five years, at least 24 case-control studies looking at the association of talc and ovarian cancer, both invasive and borderline, have been published. Studies vary in design quality and size, but show a consistent increased risk of ovarian cancer with genital talcum powder use. That data summary follows and is attached as Exhibit B.

Based on the limitations of the cohort studies and the variances in design and size of the case-control studies, I based my opinions largely on the meta-analyses, particularly Penninkilampi's most recent study. In my opinion, meta-analysis provides the most reliable evidence in this situation. The large number of overall cases (>14,000) in this study improves the power to detect a relatively small effect size. The authors agree: "As it stands, a meta-analysis of observational studies, such as the present study provides the highest level of evidence practically feasible for this research question." (Penninkilampi and Eslick 2018).

In my opinion, meta-analysis is the most valid and reliable way to study an issue like ovarian cancer, that is relatively rare and requires a long study period to detect. The cohort studies were not designed to specifically to look at talcum powder. Instead, the use of talcum powder is only one of many queries. All of the cohort studies are limited by failure to obtain complete information, lack of power, selection bias, and short follow-up.

When looking at epidemiological studies with a critical eye and in their totality, they demonstrate a clear, consistent, and statistically significant increased risk of EOC (approximately 20-50%) with the genital use of talcum powder products. This risk is replicated over a large number of case-control studies, one cohort study, and all meta-analyses/pooled analyses over several decades. Recall and confounding bias in case-control studies appear to have minimal impact. (Penninkilampi and Eslick 2018; Langseth et al. 2008). There appears to be no significant publication bias. (Berge et al. 2017; Penninkilampi and Eslick 2018).

MECHANISM

How Talc Particles Reach the Tube, Ovary and Peritoneum

In 1971, Henderson, et al of Cardiff, Wales published their findings of talc deeply embedded in ovarian cancers. (Henderson et al. 1971)(Talc was also demonstrated in cervical cancers, endometrial cancers and non-diseased ovaries.) Ten years previously, Egli and Newton had demonstrated that carbon particles instilled in the posterior vaginal fornix would be "flushed" from the fallopian tubes removed transabdominally (No propulsive force of talc introduction was used in this study). (Egli and Newton 1961). Glove powder from vaginal examination can be found in the peritoneal cavity one to four days after exam. (Sjösten, Ellis, and Edelstam 2004). Based on the studies of Egli and others, Dr. J. Donald Woodruff began to postulate that "some agent enters the peritoneal cavity through the fallopian tube, irritates the pelvic peritoneum,

produces proliferation and with an added unknown ingredient results in the development of malignancy.” (Woodruff 1979). Dr. Woodruff emphatically encouraged more scientific attention to agents introduced into the vaginal canal. This paper is the text of a lecture delivered in October of 1978. Drs. Longo and Young expressed their concerns about talc and pathogenesis of ovarian cancer and also encouraged further study of the risks of cosmetic talc use in women. (D. L. Longo and Young 1979). Although I reviewed the small number of articles that dispute talcum powder’s ability to reach the tubes and ovaries, I rejected these claims. It is a universally accepted phenomenon by the gynecologic medical community, well documented in the scientific and medical literature, that the female genital tract functions as a conduit for foreign material to enter the peritoneal cavity. This is the process that occurs with talcum powder.

How Inflammation Leads to Mutagenesis and Cancer

“Prolonged chemical exposures, persistent foreign bodies, recurrent acute inflammation or certain pathogens are all causes of chronic inflammation.” (Ferguson, Chronic inflammation and mutagenesis, 2010). In this milieu, cytokines are generated, particularly TNF-alpha and IL-1beta. These cytokines generate reactive oxygen species (ROS) and reactive nitrogen species (RNS). ROS are incompletely reduced oxygen compounds that travel through the cell hungrily seeking electrons to steal or donate. These TNF-alpha radicals are potent mutagens and are comparable to the effects of ionizing radiation. (Yan et al. 2006; Yan, Peng, and Li 2009) (Yan methods described in 2009 book chapter). These ROS radicals cause DNA breaks, DNA adducts as well as having epigenetic effects (for example, lysine acetylation in chromosomal histones). The generation of TNF-alpha is DNA synthesis dependent and occurs in the macrophage (a WBC first responder in inflammation). (Liou and Storz 2010; Ferguson 2010; Yan 2011).

Inflammation and its involvement in the etiology and development of many types of cancer, has been studied extensively. (Klampfer 2011).

The inflammatory basis for cancer development is also supported by studies showing a reduced risk of cancer with the use of anti-inflammatory agents. (Burn et al. 2011).

This inflammatory cascade has been shown to occur in the pathogenesis of EOC as well. (Shan and Liu 2009; Saed, Morris, and Fletcher 2018; Saed, Diamond, and Fletcher 2017, 2017; Saed et al. 2018; Khan et al. 2011; Trabert et al. 2014).

In the “normal” cell, DNA damage is either repaired or the damaged cell is directed via the P53 pathway to apoptosis. Yan et al (2006) found more DNA aberrations in homozygous p53-negative cells of colon cancer origin. (Yan et al. 2006). Gates et al (2008) document absence of some DNA repair mechanisms in patients who are genital talc exposed compare to controls in New England Case Control Study as well as the Nurses’ Health Study. (Gates et al. 2008).

In an *in vitro* study by Shukla (2009), crocidolite asbestos and non-fibrous talc caused expression of different genes in mesothelial cells and ovarian epithelial cells producing inflammatory cytokines. (Shukla et al. 2009).

Buz’Zard transformed normal ovarian epithelial cells to malignant cells by talc exposure. (2007). (Buz’Zard and Lau 2007). Her methods are supported by the works of Yan et al and Khan et al.

Harper and Saed have recently reported a mechanism by which talc enhances the pro-oxidant state in normal [ovarian and tubal] and ovarian cancer cells, through inductions of gene point mutations (SNPs) in key oxidant enzymes, altering their activities. (Harper and Saed 2019).

Multiple investigators have looked at the effects of aspirin and nonsteroidal anti-inflammatory drugs (NSAIDs) on the risk of developing ovarian cancer. Although somewhat inconsistent, data regarding NSAID and aspirin use suggest a protective effect (results of these studies are inconsistent. (Murphy et al. 2012; Trabert et al. 2014, 2019). In a case control study, use of NSAIDs increased the risk of ovarian cancer. (A. H. Wu et al. 2009). Trabert et al pooled 12 population based case-control studies regular aspirin use decreased the risk of ovarian cancer, both low dose and high dose. Daily high dose NSAIDs decreased ovarian cancer risk. (Trabert et al. 2014). Trabert et al looked at 15 prospective cohort studies from North America and Europe and found no effect of aspirin or NSAIDs on ovarian cancer risks. (Trabert et al. 2019). No study found an effect on ovarian cancer of acetaminophen use, an analgesic, antipyretic with no anti-inflammatory properties. Dixon et al found no correlation with pre-diagnosis aspirin or NSAID use and survival duration after the diagnosis of ovarian cancer. (Dixon et al. 2017)

ASBESTOS AND OTHER CONSTITUENTS

There is evidence from medical literature that talcum powders are not pure talc, but contain impurities including asbestos. (Cralley, Key, et al. 1968; Cralley, Keenan, et al. 1968; Rohl et al. 1976; Werner 1982; Locky 1981; Paoletti et al. 1984; Blount 1991). I have also seen evidence of testing of Johnson and Johnson talcum powder products by Dr. William Longo demonstrating the presence of asbestos and fibrous talc in talcum powder product samples. (W. E. Longo and Rigler 2018). In addition, I have seen numerous Johnson and Johnson testing results showing the presence of asbestos in their talcum powder products. (Exhibit 28, Deposition of John Hopkins, Ph.D., MDL No. 2378, 2018; Exhibit 47, Deposition of Julie Pier, MDL No. 2738, 2018).

Asbestos is well known to be one of the most potent human carcinogens. The International Agency for Research in Cancer (IARC) has determined that asbestos causes mesothelioma and cancer of the lung, larynx, and ovary. IARC 2012. According to IARC, all forms of asbestos (chrysotile, crocidolite, amosite, tremolite, actinolite, and anthophyllite and talc containing asbestiform fibers (fibrous talc) are carcinogenic. The IARC Working Group found that a “causal association between exposure to asbestos and cancer of the ovary was clearly established, based on five strongly positive studies in women with heavy occupational exposure to asbestos. (Acheson et al. 1982; Wignall and Fox 1982; Germani et al. 1999; Berry, Newhouse, and Wagner 2000; Magnani et al. 2008; IARC 2012). The IARC 100C Working Group was convened in 2009, with results published in 2012.

In 2011, Camargo et al, published a meta-analysis of epidemiologic studies of ovarian cancer in asbestos exposed women. (Camargo et al. 2011). Their finding of a standardized mortality ratio (SMR) of 1.77 for risk of ovarian cancer mortality (95% confidence intervals 1.37-2.28) corroborate the finding of the IARC Working Group.

Distinction of peritoneal mesothelioma and ovarian carcinomatosis can be difficult. Even with such discrimination, asbestos increases ovarian cancer risk. (Alison Reid, Klerk, and Musk 2011).

“Consumer products are the primary sources of exposure to talc for the general population. Inhalation and dermal contact (i.e. through perineal application of talcum powders) are the primary routes of exposure”. (IARC 2012). The mechanism of carcinogenesis of asbestos is the same as discussed above: induction of the inflammatory cascade resulting in mutagenesis either through a direct or indirect mechanism. Although migration/transport through the genital tract is the primary source of exposure with genital talcum powder use, inhalation represents a secondary exposure route. With either route, talcum powder particles can be also absorbed and transported through the lymphatics or blood system to pelvic organs and lymph nodes. The mechanism for the carcinogenicity of asbestos in the ovary and elsewhere provides a plausible biological mechanism by which it can contribute to the carcinogenicity of talcum powder products.

I have also seen evidence of the presence of heavy metals, including nickel, cadmium, and cobalt in Johnson and Johnson talcum powder products. (Exhibit 47, Deposition of Julie Pier, MDL 2738, 2018). Nickel and chromium are Group 1 carcinogens. (IARC 2012). Cobalt is identified by IARC as Group 2b possibly carcinogenic. (IARC 2012). The mechanism of action described by IARC, is inflammatory in nature. These heavy metals likely contribute to the carcinogenicity of talcum powder products by the inflammatory mechanism described at length in this report.

I have reviewed the list of fragrances chemicals contained in Johnson’s Baby Powder and Shower to Shower products and the expert report of Dr. Michael Crowley. I agree with Dr. Crowley’s opinion that these chemicals likely contribute to the inflammatory properties, toxicity and/or carcinogenicity of these products.

DETERMINATION OF CAUSATION

In 1965, epidemiologist Sir Austin Bradford Hill published his factors for determining causation from associations found in epidemiologic studies. (Hill 1965). These factors have been widely used, but are not considered absolute or required for a causal determination. These considerations have also been elaborated upon for the 21st century by Fedak et al. (Fedak et al. 2015). For a doctor treating patients, knowledge of risk factors and causes of diseases are important for diagnosis, prevention, and treatment of the diseases. In essence, risk factors (associated with a health outcome) can be considered causal when the biological and molecular mechanisms for this relationship are known or predictable based on scientific research. The following are the Bradford Hill considerations and my analysis as they relate to talcum powder products and their relationship with ovarian cancer.

Strength: There is no set magnitude or threshold for ascribing causality. I would maintain that any practice or element that increases the risk of ovarian cancer by ANY consistent percentage is significant. Ovarian cancer is, usually, a fatal disease, not a trivial inconvenience. The increased risk of ovarian cancer in perineal talc users in epidemiologic studies is 1.2-1.5, a 20-50% increased risk.

Consistency: The consistency of the case-control epidemiologic studies the uniformity of the meta-analyses (Harlow et al, 1992, Gross and Berg, 1995, Cramer et al 1999, Huncharek et al 2003, Langseth et al, 2008, the pooled study of Terry et al 2013, and the recent Penninkilampi 2017) is impressive. The studies are from different populations across three continents. The seeming inconsistency with the cohort studies are likely due to lack of power and other study design limitations. (Narod 2016). Strength and consistency are very important to a physician involved in patient care.

Specificity: Bradford Hill noted that different agents may cause more than one disease. Furthermore, any disease may have multiple component causes. “One-to-one relationships are not frequent”. (Hill 1965). Certainly, talc causes talcosis and medically induced pleural inflammation. The body of epidemiologic work supports talcum powder’s role in risk of epithelial ovarian cancer. For a physician, this consideration is less important than strength of association and consistency.

Temporality: This requirement is met by studies of risk of ovarian cancer for those who used talcum powder versus those who did not. It may take in vitro studies to establish threshold dose exposures. Bradford Hill did not address latency which is another marker of temporality. In the case of talcum powder use and ovarian cancer, the average latency period exceeds twenty years. (Magnani et al. 2008; A. Reid et al. 2014; Okada 2007). Reverse temporality is most unlikely in this case. Temporality is not particularly important to a physician as long as it has been shown to exist.

Biologic gradient: This refers to dose response relationship which is not seen in all of the epidemiologic studies, but is demonstrated in some. (Harlow et al. 1992; S. Chang and Risch 1997; Daniel W. Cramer et al. 2016; Schildkraut et al. 2016; Terry et al. 2013; Penninkilampi and Eslick 2018). In the studies that failed to demonstrate a clear dose response, many simply did not have adequate data to assess. With genital talcum powder use, quantifying exposure is challenging in terms of measuring the exact amount used in each application, the amounts that migrate or are transported through the genital tract, the amount inhaled, and the amount absorbed through the vaginal mucosa. It is also impossible to measure how much of each constituent is present in any application. In vitro studies would help clarify dose response relationships and mechanisms. To a physician, dose response can be helpful when determining causality, but not essential.

Plausibility: The growing body of evidence from in vitro studies enhance the plausibility of talcum powder’s role in the causation of ovarian cancer. The talcum powder reaches the tubes, ovaries, and peritoneum by migration/transport of particles as described earlier in this report. Once there, these particles create a hostile inflammatory environment of reactive oxygen and reactive nitrogen species capable of causing mutagenesis/carcinogenesis. This general mechanism is not only plausible, but accepted widely - even though the details at the molecular level are still being clarified. I placed a great deal of importance on the mechanism consideration and I find it compelling.

Coherence: As Bradford Hill stated, assessing causation “should not seriously conflict with the generally known facts of natural history and biology of disease”. (Hill 1965). This consideration has been satisfied, since talcum powder and its causal relationship with ovarian cancer is compatible with our knowledge of cancer and cancer processes.

Experiment: Sir Bradford Hill discussed this point as an experimental change in the epidemiologic milieu which mitigated the statistical finding. Fedak et al interpret this point in a more contemporary way: biochemical, in vitro experiments and laboratory investigation of genetic and epigenetic pathways. (Fedak et al. 2015). In this context, there is a growing body of evidence to support the biologic, genetic and epigenetic consequences to the ovarian epithelial cell with talcum powder exposure. (Shukla et al. 2009; Fletcher, Nicole, Memaj, Ira, and Saed, Ghassan 2018; Saed, Morris, and Fletcher 2018; Buz’Zard and Lau 2007).

Analogy: Sir Bradford Hill suggested the analogy of rubella and thalidomide causing birth defects in a similar fashion. I would suggest the analogy of asbestos causing ovarian cancer and mesothelioma or HPV causing cervical cancer.

I give precedence to strength of association and consistency as most important factors. If these are met, I judge plausibility and experiment next in importance.

Cornstarch as a safer alternative

Talc has been known to be more inflammatory and toxic than starch products for decades. (Eberl and George 1948). In addition, there is no epidemiological evidence linking cornstarch to ovarian cancer. (S. Chang and Risch 1997; Daniel W. Cramer et al. 2015; Cook, Kamb, and Weiss 1997). Whysner and Mohan reviewed the literature regarding talc and cornstarch and their relationship to epithelial ovarian cancer. The authors concluded that: 1) due to the chemical nature of cornstarch, a biological mechanism by which cornstarch could cause ovarian cancer is implausible; 2) epidemiologic studies have found no association between cornstarch and ovarian cancer; and 3) no increased risk of ovarian cancer from perineal cornstarch use is predicted. (Whysner and Mohan 2000).

Conclusions

In my opinion, talcum powder products cause epithelial ovarian cancer. This opinion is based on my assessment of the totality of the epidemiologic data presented in the medical and scientific literature, the biologic mechanism, and the credible presence of known carcinogens in the products. This assessment was made by analyzing and weighing the extensive evidence in the context of Bradford Hill considerations.

Summary of my opinions:

1. Johnson and Johnson talcum powder products cause the development and progression of epithelial ovarian cancer.
2. There is credible evidence that Johnson and Johnson baby powder products contain asbestos. Asbestos and fibrous talc cause epithelial ovarian cancer. Heavy metals and

fragrance chemicals added to the products can also contribute to the carcinogenicity of Johnson & Johnson Baby Powder and Shower to Shower products.

3. Talc and asbestos create an inflammatory pro-carcinogenic environment in the human body, the mechanism for epithelial ovarian cancer development and progression.
4. Perineal application of talcum powder products results in the tubal and intraperitoneal deposition of talc and asbestos by migration and transport through the genital tract. Inhalation is a secondary route of exposure.

I reserve the right to amend or modify the report as new information becomes available.

I have not testified in litigation over the previous 4 years. I am charging \$600 per hour for my work on this matter. Additional materials I considered are attached as Exhibit C.

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Exhibit A

CURRICULUM VITAE
Ellen Blair Smith, M.D.

PERSONAL DATA:

Birth Date: December 9, 1951

Mailing Address: 2311 Camino Alto Road
Austin, Texas, USA 78746

Email: ellenblairsmith@gmail.com

NPI: 15583054

Employment Status: Retired from Texas Oncology, PA December 31, 2015
Medical director, Halcyon Home Hospice, April, 2017-present

EDUCATIONAL HISTORY:

1969: Diploma, Grimsley High School, Greensboro, North Carolina
1971: A.A. , St. Mary's Junior College, Raleigh, North Carolina
1973: B.A. Biology, University of North Carolina, Greensboro. North Carolina
1977: M.D., University of North Carolina. Chapel Hill, North Carolina

SCHOLASTIC HONORS:

1974 Mosby Award
1976 Merck Award
1976 Student Aptitude Award, North Carolina Society of Obstetrics and
Gynecology
1976 Alpha Omega Alpha, University of North Carolina School of Medicine
1977 American Medical Women's Association Citation of Scholastic
Achievement

POSTGRADUATE TRAINING:

1977-1978: Internship, Obstetrics and Gynecology, UTHSCSA, San Antonio, Texas
1978-1981: Residency, Obstetrics and Gynecology, UTHSCSA, San Antonio, Texas
1979: Galloway Fellowship, Memorial Sloan-Kettering, NY, NY
1981-1984: Fellowship, Gynecologic Oncology, Duke University Medical School,
Durham, NC (1983: American Cancer Society Fellow)

PREVIOUS EMPLOYMENT:

1984-1987: Assistant Professor, Gynecologic Oncology, University of Virginia Medical
School, Charlottesville, Virginia
1987-1989: Physician and Sole Proprietor, Gynecologic Oncology, Austin, Texas
1989-1995: Physician and President, Austin Gynecologic Oncology Associates, Austin, TX

CURRICULUM VITAE

Ellen Blair Smith, M.D.

1995-2008: Physician and Partner, Southwest Regional Cancer Center, Austin, Texas

2008-2015: Physician Shareholder, Texas Oncology, Austin, Texas

MEDICAL LICENSURE:

Texas Medical Board: F0313 (active)

DEA: AS 1121021 (active)

Texas DPS 40063099 (active)

North Carolina State: 24537 (inactive)

Virginia State: 10103669 (inactive)

BOARD CERTIFICATIONS:

1985 American Board of Obstetrics and Gynecology (lifetime certified, voluntary
recertification 1996)

1987 American Board of Obstetrics and Gynecology, Division of Gynecologic Oncology
(lifetime certified, voluntary recertification 1996)

2011 Hospice and Palliative Medicine (via ABOG), expires 2021

APPOINTMENTS:

1981-1982 Associate, Obstetrics and Gynecology, Duke University Medical School,
Durham, NC

1982-1984 Assistant Professor, Obstetrics and Gynecology, Duke University Medical
School, Durham, NC

1984-1987 Assistant Professor, Department of Obstetric and Gynecology, University
of Virginia Medical Center, Charlottesville, VA

1997-2000 Renaissance Women's Center Advisory Board, Austin, Texas

1998-2003 Hospice Austin Medical Advisory Board, Austin, Texas

1999-2001 Mediation Committee, Travis County Medical Society, Austin, Texas

2001-2007 Gynecologic Cancer Foundation, Board of Directors

Nominating Committee Chair 2004

2007-2008 Section Chief Ob-Gyn, Seton Medical Center, Austin, Texas

2007-2014 Member Surgical Committee, Seton Medical Center, Austin, Texas

2011-2013 Medical Director of Surgical Services, US Oncology (elected office)

2011-2013 Member, National Policy Board Executive Committee, US Oncology

2011-2015 Member, Managed Care Committee, US Oncology

2011-2015 Member, Pathways Committee, US Oncology

PROFESSIONAL SOCIETIES:

Alpha Omega Alpha (1976-current)

American Cancer Society

1985-1987 Charlottesville-Albemarle Unit

Board of Directors

Executive Committee

1984-1986 Virginia Unit

CURRICULUM VITAE

Ellen Blair Smith, M.D.

Board of Directors
Colorectal Cancer Control Project Steering Committee
Finance Committee 1986
Nominating Committee 1986
1987-1988 Austin, Texas Unit
Public Education Chairman
American Congress of Obstetrics and Gynecology (1988-Life Member)
Society of Gynecologic Oncology (1988-lifetime)
Program Committee 1995-1996
Coding Committee 1996-2001
Nominating Committee 2008
Palliative Care Committee 2009-current
Session Moderator-Palliative Care- SGO Annual Meeting-2014
Steering Committee, SGO Genetics Summit-2015
American Academy of Hospice and Palliative Medicine 2010-present

PUBLICATIONS (PEER-REVIEWED JOURNALS) :

Smith, EB, Weed, JC, Tyrey, L and Hamond, CB: "Treatment of Nonmetastatic GTD: Results of Methotrexate-Folinic Acid." *Amer J Obstet Gynecol*, 144:88, 1982.

Smith, EB, Szulman, AE, Hinshaw, W, Tyrey, Surti, U, and Hammond, CB: "Human Chorionic Gonadotropin Level in Complete and Partial Hydatidiform Moles and Nonmolar Abortuses." *Amer J Obstet Gynecol*, 149: 129, 1984.

Smith, EB, Clarke-Pearson, DL, and Creasman, WT: "A VP-16 and Cis-Platinum Containing Regimen for Treatment of Refractory Ovarian Germ Cell Malignancies" *Amer J Obstet Gynecol*, 150:927, 1984.

Smith, EB, Dunnick, R, Nelson, PA and Hammond, CB: "Renal Metastases of Malignant Gestational Trophoblastic Disease with Particular Attention to the Use of Intravenous Urography in Staging." *Gynecol Oncol* 20: 137, 1985.

Barter, J, **Smith, EB**, Szpak, CA, et al: "Leiomyosarcoma of the Uterus: A Clinicopathologic Study of 21 Patients." *Gynecol Oncol* 21:221, 1985.

Puleo, JG, Clarke-Pearson, DL, **Smith, EB**, Barnard, DE, and Creasman, WT: "Superior Vena Cava Syndrome Associated with Gynecologic Malignancy." *Gynecol Oncol* 23:59, 1986.

Taylor, PT, Anderson, WA, Barber, SR, Covell, JL, **Smith, EB**, and Underwood, PB: "The Screening Papanicolaou Smear: Contribution of the Endocervical Brush." *Obstet Gynecol* 70:734, 1987.

Anderson, WA, Found, D, Peters, W, **Smith, EB**, Bagley, C and Taylor, PT: "Platinum-Based Combination Chemotherapy for Malignant Mixed Mesodermal Tumors of the Ovary." *Gynecol Oncol* 32: 319, 1989.

Plante, M, **Smith, EB** et al: "The case of a viable pregnancy post vaginal radical trachelectomy followed by combined chemoradiation." *Gynecol Oncol* 123:421, 2011.

CURRICULUM VITAE
Ellen Blair Smith, M.D.

PUBLICATIONS (INVITED ARTICLES AND BOOK CHAPTERS):

Creasman, WT, **Smith, EB** and Clarke-Pearson, DL: "Gestational Trophoblastic Disease." *The Female Patient*, 9:66, 1984.

Smith, EB, Clarke-Pearson, DL, and Creasman, WT: "Screening of Cervical Cancer." (Chapter10) *Screening and Monitoring of Cancer*. Basil A Still, ed. John Wiley & Sons; 1985.

Smith, EB and Creasman, WT: "Preinvasive and Invasive Cervical Carcinoma Associated With Pregnancy." *Principles of Medical Therapy in Pregnancy*. N Gleicher, ed. Plenum Publishing Corp. New York, New York. 1985. Revision 1990.

Smith, EB, Hammond, CB, Gore, H and Hertig, A. "Gestational Trophoblastic Disease". *Management of the Patient with Cancer*. 3rd edition. TF Nealon, ed. W. B. Saunders CO, Philadelphia, Pa. 1986.

Smith, EB: "Gynecology for the Urologist." *Adult and Pediatric Urology*. J Gillenwater. ed. Year Book Medical Publishers; 1987. Revision 1991.

INVITED LECTURES:

SGO State of the Art Meeting 2011- Palliative Care

SGO Winter Meeting 2013-Palliative Care

Exhibit B

First author and year	Cases (%talc use)	Controls (%talc use)	OR	95% CI	Dose Response	Comments
Cramer, 1982	215 (43%)	215 (28%)	1.9	1.27-2.89		
Hartge, 1983	135	171	0.7	0.4-1.1		hosp, letter only. Only 10 with perineal use
Whittemore, 1988	188 (52%)	539 (46%)	1.45	0.81-2.8	no	perineal use, mixed hosp and population
Harlow, 1989	116	158	2.8	1.111-7	no	LMP only, deodorant powder +/- talc
Booth, 1989	235 (68%)	451 (61%)	rare=0.9 weekly=2.0 daily=1.3	0.3-2.4 1.3-3.4 0.8-1.9	no	hosp. path reviewed
Rosenblatt, 1992	77 (91%)	46	1	0.2-4.0		These nmbers are way too small.
Chen, 1992	112 (6%)	224 (2%)	3.9	0.9-11.6		also used occupational exposure, only 7 vs 5 total perineal powder users
Harlow, 1002	235 (48 5%)	239 (39.3)	1.5	1.0-21	trend NSS	perineal use
Tzounou, 1993	189 (3%)	200 (3 5%)	1.05	0.28-3.98		hosp, hairdye, low usage numbers, Greece
Purdie, 1995	824 (57%)	860 (52%)	1.25	1,04-1,54		adj for parity , 17% LMP Austrailia
Shusan, 1996	200 (11%)	406 (5.6%)	seems to be : simple X2= 0.4			Never/seldom vs mod-a lot, Focus on fertility drugs Israel
Chang, 1997	450 (44%)	564 (35.6%)	all 1.42 LMP 1.24 inv 1 51	1.08-1.86 0.76-2.02 1.13-2.02	duration=borderline frequency=no	no assn with cornstarch, Canada
Cook, 1997	313	422	1.5	1.1-2.0	no	ever powder use, looked at genital deodorant as well
Godard, 1998	170 (10.6)	170 (4.7)	2.49	0.94-6.56		perineal use only p=0.066 French Canadians
Wong, 1999	499 (47 8%)	755 (44.9%)	genital+pad 1.1 genital 1.0 pad 0 9	0.7-1.7 0.8-1.3 0.4-2.0	no	

first author, year	cases (% talc use)	controls (%talc use)	OR	95% CI	dose-response	Comments
Cramer, 1999	563 (45%)	523 (36%)	any genital powder 1.6 perineal talc 1.69	1.18-2.15 1.26-2.27	no	
Ness,2000	767 (55%)	1367 (47%)	genital 1.5 pad 1.6	1.1-2.0 1.1-2.3	no	BTL protective, risk increased witalc on all areas body
Mills,2004	256 (43%)	1122 (37%)	ever talc 1.37 serous 1.77	1.02-1.85 1.12-1.81	no	
Merritt, 2008	1576 (46%)	1509 (43%)	1.17	1.01-1.36		adjusted OR, decreased with ASA, BIG NUMBERS Australia includes LMP, FT, PP
Moorman,2009	143 AA 943 white	189 AA 868 white	1.19 1.04	0.68-2.09 0.82-1.33)		
Rosenblatt, 2011	812	1313	all 1.27 LMP 1.55 inv 1.38	0.97-1.66 1.02-2.37 0.77-2.47	no	
Kurtha, 2012	902 (22%)	1802 (20.9%)	1.4	1.16-1.69		The definitive fertility drug risk paper
Wu, 2015	hispanics 308 (38%) AA 128 (48%) white 1265 (41%)	380 (28%) 143 (44%) 1868 (30%)	1.56 1.77 1.41	0.8-3.04 1.20-2.62 1.21-1.67		Stat sig more talc use in Aas
Cramer, 2016	2014 (51%)	2100 (48%)	1.33	1.16-1.52	trend for freq none for duration	
Schildkraut,2016	584 (63%)	745 (53%)	1.44	1.11-1.86	yes	

Exhibit C

- “A Survey of the Long-Term Effects of Talc and Kaolin Pleurodesis.” *British Journal of Diseases of the Chest* 73 (1979): 285–88. [https://doi.org/10.1016/0007-0971\(79\)90054-8](https://doi.org/10.1016/0007-0971(79)90054-8).
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- . "Genital Use of Talc and Risk of Ovarian Cancer: A Meta-Analysis." *European Journal of Cancer Prevention: The Official Journal of the European Cancer Prevention Organisation (ECP)* 27, no. 3 (2018): 248–57. <https://doi.org/10.1097/CEJ.0000000000000340>.
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Exhibit 5

**UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY**

**IN RE JOHNSON & JOHNSON
TALCUM POWDER PRODUCTS
MARKETING, SALES PRACTICES,
AND PRODUCTS LIABILITY
LITIGATION**

MDL NO. 16-2738 (FLW) (LHG)

THIS DOCUMENT RELATES TO ALL CASES

**RULE 26 EXPERT REPORT OF
DANIEL L. CLARKE-PEARSON, MD**

A handwritten signature in cursive script that reads "Dan Clarke-Pearson MD".

Date: November 16, 2018

Daniel L. Clarke-Pearson, MD

Daniel L. Clarke-Pearson, MD
Robert A. Ross Distinguished Professor and Chair
Department of Obstetrics and Gynecology
University of North Carolina, Chapel Hill

Background and Qualifications

I am certified by the American Board of Obstetrics and Gynecology as a specialist in obstetrics and gynecology as well as a subspecialist in gynecologic oncology. The focus of my clinical practice, teaching and research for the past 40 years has been the care of women with gynecologic cancers (cancers of the ovary, fallopian tube, uterus, cervix, vagina, and vulva). In addition, I also provide care for complex gynecologic surgical problems (endometriosis, large ovarian tumors, leiomyomata).

I received a BA from Harvard College (major in biology). I spent a year as a laboratory technician developing a device to noninvasively detect deep venous thrombosis. I then attended medical school at Case Western Reserve University School of Medicine (Cleveland, OH). After graduating in 1975, I completed a four-year residency in Obstetrics and Gynecology at Duke University Medical Center (Durham, NC). I then completed a three-year fellowship in Gynecologic Oncology at Duke. From 1982-1985 I was an assistant professor on the Duke faculty (Division of Gynecologic Oncology). From 1985-1987 I was the Director of Gynecology and Gynecologic Oncology at the University of Illinois (Chicago, IL). I returned to Duke in 1987 to serve as the Director of Gynecologic Oncology and Director of the Gynecologic Oncology Fellowship program. I was appointed a full professor with tenure and was awarded a Distinguished Professorship (James Ingram Professor of Gynecologic Oncology) in 1993.

In 2005, I was appointed Chair of the Department of Obstetrics and Gynecology at the University of North Carolina (Chapel Hill, NC). As the Robert A. Ross Distinguished Professor and Chair, I have administrative responsibilities over 75 faculty, 28 residents in obstetrics and gynecology and 29 fellows receiving subspecialty training in eight subspecialties. I have continued to provide clinical care to women with gynecologic cancers including surgery, administration of chemotherapy, conducting clinical trials and educating residents in Obstetrics and Gynecology and Fellows in Gynecologic Oncology.

I have published over 200 peer-reviewed manuscripts in the medical literature. I have also written over 50 chapters for medical textbooks and edited three medical textbooks. My research has focused on the treatment of gynecologic cancers, surgical techniques, and the prevention of venous thromboembolic (VTE) disease. I have conducted the practice defining clinical trials evaluating various methods to prevent VTE in gynecologic surgery. I have served on the editorial boards of two peer-review journals (*Obstetrics and Gynecology* and *Gynecologic Oncology*). I served as a board examiner for the American Board of Obstetrics and Gynecology for eighteen years.

I have been actively involved with relevant medical organizations including the American College of Obstetricians and Gynecologists (ACOG), the Society of Gynecologic Oncology (SGO), the American College of Surgeons (ACS) and the Gynecologic Oncology Group (GOG). I have lead numerous postgraduate continuing education courses sponsored by ACOG. Most have focused on teaching obstetricians and gynecologists complex pelvic surgery and management (and prevention) of surgical complications. I have served on several ACOG committees (Technical Bulletins, Gynecologic Management and Grievance) and was the chair of the Gynecologic Management Committee that wrote Clinical Opinions distributed to ACOG members. I also served a three-year term on the ACOG Executive Board. As a gynecologic oncologist, I have been an active member of the SGO and have served on a number of SGO Committees and the Executive Board. In 2010, I was the SGO President. As a member of the American College of Surgeons, I have presented CME lectures at the ACS annual meeting and have served on the ACS Obstetrics and Gynecology Advisory Committee. I am currently a member of the ACS Commission on Cancer. The GOG is a cooperative group organization sponsored by the National Cancer Institute to conduct clinical trials investigating new treatments to improve the outcomes of women with gynecologic cancers. Many of the publications on my CV (Exhibit A) derive from participation in these clinical trials.

Currently, I am a member of the SGO Ethics Committee and the President of the Council of University Chairs of Ob Gyn (CUCOG).

Materials and Methods

I was asked to provide opinions on these questions: 1) Can the use of talcum powder in the perineal area cause epithelial ovarian cancer? and 2) If so, what is the biological mechanism for this occurrence?

To answer these questions and prepare this report, I sought to obtain relevant information through several sources. I primarily relied on a PubMed search of "talc AND Ovarian Cancer", "Ovarian Cancer AND risk factors", "Talcum Powder AND Ovarian Cancer", "Talcum Powder AND Cancer", "Talc AND Cancer", "Asbestos AND Ovarian Cancer", "Asbestos AND Cancer". These searches provided peer-reviewed papers that included original research, case-controlled studies, cohort studies, meta-analysis studies, and review papers and systematic analysis. I also searched some of the references cited in these papers. Google searches were also performed. I also reviewed a number of textbooks searching for "ovarian cancer risk factors" and "talc/talcum powder". In addition to my literature review, I received relevant materials at my request to clarify a particular topic or answer a question. I approached this research with the same scientific rigor that I would use in my own clinical, academic, and research practice.

I assessed the data and conclusions of these peer-reviewed articles considering the strengths and weaknesses of each particular study. The medical and scientific literature on these topics varies in the quality of the study design and, at times, in conclusions. I approached each article objectively and critically, assessing for factors such as design, power, reputation of author(s),

quality of journal, and potential biases. The increased risk associated with the genital use of talcum powder is consistently described over decades. When formulating my opinions regarding causality, I considered the extensive body of literature in its totality, weighing the data and information according to its importance using the concepts outlined by Bradford Hill. Overall, I believe that the opinions expressed in this report are strongly supported by credible scientific research.

Overview of Ovarian Cancer

Approximately 22,000 women in the US will be diagnosed with ovarian cancer annually. To date, there is no method to screen for ovarian cancer and symptoms associated with ovarian cancer are vague and not specific. Therefore, at the time of initial diagnosis, nearly 75% of women will have ovarian cancer spread throughout the abdominal cavity and into the lung (pleural effusion). Current treatment includes initial surgery to attempt to remove the bulk of the cancer (“debulking surgery”) followed by treatment with multi-agent chemotherapy. Unfortunately, the majority of women will ultimately die from this malignancy. The most common histologic type of ovarian cancer is high-grade serous cancer, also termed “epithelial ovarian cancer” (EOC).

Pathogenesis of Ovarian Cancer

There are several theories as to the origin of ovarian cancer. One holds that “incessant ovulation” requires “repair” of the ovarian surface epithelium after each ovulation. The “repair” mechanism is prone to generate DNA errors (mutations) that result in malignant transformation. (Fathalla 1971). This theory is supported by observations that events that reduce ovulation are associated with a lower risk of a woman developing ovarian cancer. (Pregnancy, breast feeding, use of oral contraceptives all reduce the risk of ovarian cancer). (Havrilesky et al. 2013; La Vecchia 2017).

Before 2008, it was presumed two other cancers in women (fallopian tube and primary peritoneal) were distinct from ovarian cancer. However, Levanon recognized that many EOCs actually arise in the fallopian tube and metastasize to the ovary and peritoneal cavity. (Levanon, Crum, and Drapkin 2008). This observation is supported by molecular data (especially the frequent finding of P53 mutations in the fallopian tube and EOC metastases. (Fathalla 2013; Kurman and Shih 2016; Dubeau and Drapkin 2013; Chien et al. 2015). Today, we believe that EOC, fallopian tube carcinoma and primary peritoneal carcinoma are the same entity and share similar risk factors and pathogenesis.

By definition, cancer results from gene mutations in normal cells that transform the normal cell into a cell that has lost its regulation of controlled growth. Mutations can occur through a number of processes. Some mutations may be inherited from either the patient’s mother or father. BRCA1, BRCA 2 and mismatch repair gene (Lynch Syndrome) mutations are such examples. In most instances, the mutations occur due to exposures such as virus (HPV virus causing cervix, anal, vulvar and oropharyngeal cancers), tobacco smoking (lung cancer) and

exposure to x-rays (leukemia). Some exposures result in a chronic inflammatory response that induces mutations as the normal cell attempts to repair damage such as that caused by asbestos (pulmonary mesothelioma, ovarian cancer). These mutations can also occur spontaneously as cells (and individuals) age. (Bottazzi, Riboli, and Mantovani 2018).

Inflammation and Cancer

There is a clear link between inflammation (resulting in oxidative stress) and cancer risk. This is true for many types of cancer including ovarian cancer. (Balkwill and Mantovani 2001; Coussens and Werb 2002; Okada 2007; Reuter et al. 2010; Crusz and Balkwill 2015; Fernandes 2015). Inflammation causes cancer through promoting cell proliferation, oxidative stress, and DNA damage and gene mutations. This process is associated with many steps in the genesis of cancers including initiation, progression, metastases and chemoresistance. Both inflammatory cells and cancers produce cytokines and chemokines that contribute to cancer growth and spread. Cytokines, particularly TNF-alpha and IL 1 beta, generate reactive oxygen species (ROS) and reactive nitrogen species (RNS). These are potent mutagens and are comparable to the cell damage caused by ionizing radiation (Yan, 2006). These ROS radicals cause DNA breaks and DNA adducts. The inflammation cascade has been shown to occur in the pathogenesis of EOC. (Shan and Liu 2009; Saed, Diamond, and Fletcher 2017; Khan et al. 2011; Saed et al. 2018; Trabert et al. 2014). Harper and Saed recently reported the induction of single nucleotide polymorphisms (SNPs) following exposure of normal ovarian and tubal cells and ovarian cancer cells to talcum powder. (Harper and Saed 2019). In a "normal cell", DNA damage may be repaired. Alternately, the damaged cell may undergo "programmed cell death" (apoptosis) as directed by the P53 pathway. (P53 is a tumor suppressor gene).

Talcum powder is known to elicit an inflammatory response in animal and humans. (Eberl and George 1948; Radic et al. 1988; "NTP Toxicology and Carcinogenesis Studies of Talc (CAS No. 14807-96-6)(NonAsbestiform) in F344/N.Rats and B6C3Fl Mice (Inhalation Studies)" 1993). Shukla demonstrated in vitro that crocidolite asbestos and non-fibrous talc caused expression of genes in ovarian epithelial cells producing inflammatory cytokines. (Shukla et al. 2009). Gates documented absence of some DNA repair mechanisms in patients who were genital talcum powder exposed when compared to controls in the New England Case Control Study. (Gates et al. 2008). In another series of in vitro experiments, Buz'Zard transformed normal ovarian epithelial cells to malignant cells by talc exposure. (Buz'Zard and Lau 2007). Yan and Kahn have demonstrated similar findings in their laboratories. (Yan et al. 2006; Khan et al. 2011).

EOC Risk Factors

Inherited mutations such as BRCA1, BRCA 2 are the most significant risk factor. The lifetime risk of developing ovarian cancer is 39-46% in BRCA1 carriers and 11-27% in women with BRCA 2 mutation. (Ring et al. 2017). This is compared to 1.3% lifetime risk in non-carriers. However, BRCA mutations only account for 10-15% of all EOC (Lancaster 2015). Women with hereditary

risk are also affected by genetic modifiers, including nongenetic and environmental factors. (Levy-Lahad 2007). In addition to talcum powder use and asbestos, other risk factors include increasing age, family history of ovarian or breast cancer, nulliparity, early menarche or late menopause, high fat diet, infertility, endometriosis, polycystic ovarian syndrome, hormone replacement therapy, IUD use, history of pelvic inflammatory disease and obesity. (Hunn and Rodriguez 2012; Mallen, Townsend, and Tworoger 2018; Park et al. 2018; Folkins et al. 2018).

Multiparity, breast feeding, oral contraceptive use, tubal ligation, salpingoophorectomy, and hysterectomy (without salpingoophorectomy) reduce the risk of developing EOC. (Hunn and Rodriguez 2012; Mallen, Townsend, and Tworoger 2018; Park et al. 2018; Folkins et al. 2018).

Talcum Powder, Asbestos and other carcinogens

During my postgraduate (residency) training (1975-1979) in obstetrics and gynecology it was reported that asbestos had been identified in ovarian cancer tissue samples (Henderson) and that talcum powder contained asbestos. It seemed plausible that asbestos (a known carcinogen) could be an EOC risk factor. However, we were taught that asbestos had been removed from talcum powder in the production process.

As a young gynecologic oncologist, it was reassuring to learn that asbestos was no longer contained in talcum powder because we knew that asbestos was a potent carcinogen. IARC monograph 100c (2012) clearly summarizes the evidence associating asbestos to cancer of the lung, larynx and ovary. Experimental models demonstrate sufficient evidence for the carcinogenicity of all forms of asbestos (chrysotile, crocidolite, amosite, tremolite, actinolite and anthophyllite) and that all forms, as well as talc containing asbestiform fibers are carcinogenic to humans. Specifically addressing the increased risk of EOC in women exposed to asbestos in occupational settings, there are at least five cohort mortality studies (Acheson et al. 1982; Wignall and Fox 1982; Germani et al. 1999; Berry, Newhouse, and Wagner 2000; Magnani et al. 2008), two population-based cohort studies (Vasama-Neuvonen et al. 1999; Pukkala et al. 2009) and a case control study (Langseth and Kjaerheim 2004) showing a causal association between exposure to asbestos and ovarian cancer.

In the late 1970s concerns that talc could be associated with EOC were expressed by Woodruff and Longo. (Woodruff 1979). The hypothesis suggested that talc applied to the perineum (vulva) ascends to the vagina and then into the uterus and through the fallopian tubes to implant on the ovary and other peritoneal surfaces. This foreign body was known to create a potent inflammatory reaction when found in the lungs, pleural cavity and peritoneal cavity. In fact, as gynecologic surgeons, we were taught to wash the talcum powder off of our surgical gloves before opening the abdomen to prevent inflammatory reactions and adhesions.

In 1982 a case-control study was the first epidemiologic study alerting the medical community of the possible association of talc use and EOC. (D. W. Cramer et al. 1982). Cramer compared women who did and did not use talc in their perineal hygiene. Regular use of talc was found to be associated with an increased occurrence of EOC by 92% (OR of 1.92. 95% confidence

interval 1.27-2.89). Cramer wrote, "It is not clear whether this derives from the asbestos content of talc or from the uniqueness of the ovary which might make it susceptible to carcinogenesis from both talc and other particulates."

Talcum powder also contains other carcinogens including asbestos, talc containing asbestiform fibers (fibrous talc), heavy metals such as nickel, chromium and cobalt (possible 2b), and other inflammatory agents, toxins, and carcinogens contained in the fragrance chemicals in talcum powder. (Expert Report of Longo and Rigler 2018; Exhibit 28, Deposition of John Hopkins, Ph.D., MDL No. 2378, 2018; Exhibit 47, Deposition of Julie Pier, MDL 2738, 2018; Expert Report of Michael Crowley, Ph.D, MDL No. 2738, 2018).

Epidemiology Studies

The association of talcum powder and EOC is based on several types of epidemiologic studies. Of course, a randomized controlled double-blinded trial would be more conclusive. However, a randomized trial would be unethical given the evidence that talcum powder causes EOC.

When looking at these epidemiologic studies in their totality, the data shows a consistent, statistically significant increased risk of developing EOC with perineal talcum powder use. Overall, the risk is increased 20-60% when compared with women who did not use talcum powder.

The original case control study published by Cramer et al in 1982 evaluated the use of perineal talcum powder in 215 white women with EOC (29 cases were "borderline" or ovarian cancer of low malignant potential). These women with EOC were matched by race, age and residence to 215 women in the same community. Talc exposure from surgical gloves, diaphragm use and perineal use was ascertained. Talc was used by 42.8% of women with EOC and only 28.4% of women who did not have EOC. Any perineal talc exposure showed a 1.92-increased relative risk of EOC (95% confidence limits 1.27-2.89). (D. W. Cramer et al. 1982).

Subsequently, there have been at least 24 other case-control studies looking at the association of talc and EOC. Overall, the case-control studies show a 30-40% increased risk of EOC associated with talcum powder use. These individual studies vary in size and quality and I weighted them accordingly. Three recent case-control studies replicated previous studies showing an increased risk of EOC in women using perineal talcum powder. Wu evaluated 1701 Californian women with EOC and found talc significantly increased the risk of EOC by 40% in whites, 20% in Hispanics and 56% in African Americans. (Wu et al. 2015). Owing to the small number of African American women in this study, the findings were not significant. Subsequently, the National Cancer Institute sponsored a multi-center study of African American women and found a 44% increase in EOC associated with talc use. A dose-response was also found for duration of use and number of lifetime applications ($p < .05$). (Schildkraut et al. 2016). Cramer performed a case control study (with additional pooled data) in 2016 that included nearly 4,000 women with EOC finding an elevated EOC risk of 33% (OR 1.33; CI....). Risk increased with frequency and duration of use. (Cramer et al. 2016).

While recent case-control studies and cohort studies are compelling, I feel that meta-analysis studies are much stronger in that they include larger numbers of patients resulting in greater statistical power. I reviewed six meta-analyses reported between 1995 and 2018. All of these studies report a statistically significant increase risk of EOC in women who use perineal talc:

Author	Years	# case control studies	Odds Ratio	95% Confidence interval
Gross & Berg	1995	9	1.27	1.09-1.48
Cramer	1999	14	1.36	
Huncharek	2003	16/11,933 subjects	1.33	1.16-1.45
Langseth	2008	14	1.40	1.29-1.52
Terry	2013	8/8,525 cases	1.24	1.15-1.33
Penninkilampi	2018	24/13,421 cases	1.31	1.24-1.39

Penninkilampi reported that there was a further increase in EOC in women who used talcum powder more frequently. In those women who had greater than 3,600 lifetime applications the odds ratio increased to 1.42 (OR 1.42; CI 1.25-1.39) when compared with women who used < 3,600 applications (OR 1.32; CI 1.15-1.50). In this study, talcum powder use was associated with an increased incidence of endometrioid and serous EOC but not mucinous or clear cell types. (Penninkilampi and Eslick 2018).

In summary, when evaluating all epidemiological studies, there is a consistent and statistically significant increased risk of developing EOC with perineal talcum powder use.

Migration

How is it possible for cosmetic talcum powder, applied to the perineum, to reach the fallopian tube and ovary and cause an inflammatory response that could result in malignant transformation?

As compared to males, the female reproductive tract is open and allows migration of potential pathogens into the peritoneal cavity. The female reproductive tract is in continuity between the peritoneal cavity and the external environment. For example, an ovum extruded from the ovary (an intraperitoneal organ) can progress down the fallopian tube to the uterine cavity, implant and result in a pregnancy that delivers vaginally. The converse is also obvious. It is clearly recognized that sperm (including sperm and sperm particles which would be non-motile) ascend from the vagina through the uterus and into the fallopian tube and into the peritoneal cavity. (Jones and Lopez 2006). Sexually transmitted bacterial infections (for example, gonorrhea and chlamydia) ascend from the vagina to the tube and ovary resulting in pelvic inflammatory disease and tubo-ovarian abscesses. While sperm and bacteria are “motile”, non-motile substances have been demonstrated to ascend from the vagina to the peritoneal cavity. As far back as 1961, Egli demonstrated that carbon particles placed in the posterior vaginal

fornix were observed in the fallopian tubes within less than one hour in two of three patients tested. (Egli and Newton 1961). Venter and Iturralde placed albumin microspheres labelled with 99mTc into the vagina. (Venter and Iturralde 1979). During pelvic surgery the following day, radioactive levels were found in the tubes and ovaries in nine of 14 cases. Sjosten conducted a trial that showed that powder on gloves use to perform a gynecologic exam resulted in powder detected in the peritoneal fluid, tubes and ovaries one day after the examination. (Sjösten, Ellis, and Edelstam 2004). Likewise, talc has been detected on the ovaries following surgical oophorectomy. (Henderson et al. 1971; Heller, Gordon, et al. 1996; Heller, Westhoff, et al. 1996).

I reviewed the small body of literature suggesting that migration of particles does not occur and do not think these studies are compelling.

I believe that ascension of talcum powder and its constituents through the genital tract is the most important route of exposure. However, inhalation is another plausible mechanism. (IARC 2012; Steiling et al. 2018). With either route, at least some of the talcum powder components are likely to be absorbed into the lymphatic system and bloodstream, representing another mechanism for exposure to internal organs.

In my opinion, genital application of talcum powder is a significant risk factor for all users and can cause epithelial ovarian cancer in some women by an accepted mechanism. As an academic and practicing physician, I made this determination in the context of Bradford Hill considerations as follow:

Strength and consistency: This opinion is supported by overwhelming epidemiologic evidence showing that the use of talcum powder statistically increases a woman's risk of developing EOC by approximately 30 percent (Odds ratio 1.31; Penninkilampi 2018). Every meta-analysis before 2018 also reported similar increase in the risk of developing EOC with the use of talcum powder. In my view, especially when considering the severity and frequency of ovarian cancer and the preventable nature of talcum powder usage, this finding is critically important and consistently supported by numerous studies.

Specificity: Based on the epidemiologic studies cited in this report, there appears to be a specific ovarian cancer caused by talcum powder: epithelial ovarian cancer (EOC). This association satisfies this consideration, although I did not weigh this factor to be as important as strength and consistency.

Temporality: In many cancers where there are identified etiologic agents (smoking and lung cancer, HPV infection and cervical cancer) there is a latency period (time from exposure to the onset of the cancer) that can extend over decades. In the case of talcum powder and ovarian cancer there is a clear latency period of decades of talcum powder use before a woman develops ovarian cancer, thus fulfilling this consideration.

Biologic Gradient/Dose-response: Measuring the “dose” of talcum powder used by an individual woman is difficult to ascertain and has been dependent on recall by the woman. In general, studies have attempted to capture the application “frequency” (daily? Only used on perineal pads during menstrual cycle?) or duration of use (how many years?). In addition, biologic gradient or dose-response is not always linear (e.g. asbestos exposure and mesothelioma is generally thought to have a “threshold response”). None the less, a number of studies have demonstrated an association between “dose” and the occurrence of EOC (response). (Terry et al. 2013; Schildkraut et al. 2016; Daniel W. Cramer et al. 2016; Penninkilampi and Eslick 2018). In modern times, molecular research is often used to elucidate this factor. I anticipate that this will occur as more in vitro studies are performed with talcum powder.

Plausibility: This is obviously a critical factor when forming opinions on causation of a risk factor. Evidence shows that talcum powder ascends from the perineum through the vagina, cervix and uterus into the fallopian tubes and onto the ovary. Talcum powder is known to be an agent that causes inflammation. An inflammatory reaction caused by talcum powder on the tube and surface of the ovary results in genetic mutations and carcinogenesis. Talcum powder causes ovarian cancer through this mechanism. The “agent(s)” that causes the inflammatory reaction and carcinogenesis may be talc, asbestos, fibrous talc, heavy metals and/or chemicals contained in fragrances added to talcum powder.

Coherence: Epidemiological data, in vitro and in vivo research are consistent in explaining the pathogenesis of EOC through the inflammatory mechanisms described above. (Saed, Diamond, and Fletcher 2017; Nadler and Zurbenko 2014). Further, this is consistent with the causes of other cancers.

Experiment: There are no randomized trials comparing outcomes of women who use or who do not use talcum powder in their perineal hygiene. Further, such a trial at this point in time would be unethical. How could we expose women to talcum powder when the existing evidence supports causation of EOC? Laboratory research (in vitro) present evidence to support the biologic, genetic and epigenetic consequence to ovarian epithelium when exposed to talcum powder. (Shukla et al. 2009; Fletcher and Saed 2018; Saed et al. 2018).

Analogy: There are numerous reports in the medical literature of minerals similar to talc causing cancer. Probably the most significant example is asbestos and lung cancer (mesothelioma).

Summary of Opinions

It is my opinion, based on research that I have conducted in the medical and scientific literature as well as my knowledge and experience as an obstetrician-gynecologist and as a subspecialist in gynecologic oncology for over 40 years, that the use of talcum powder products including Johnson’s Baby Powder and Shower to Shower, applied to the perineum of women, is a causative factor in the development of EOC. The mechanism by which talcum powder causes

cancer involves: 1) ascension of particles to the fallopian tubes and ovaries and 2) initiation of an inflammatory process that includes oxidative stress and specific genetic mutations.

These opinions are made to a reasonable degree of medical and scientific certainty.

I am being compensated for my work in this case at a rate of \$700 per hour.

I reserve the right to supplement or amend this report if new information becomes available. The materials I considered are attached as Exhibit B. My prior testimony is attached as Exhibit C.

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Exhibit A

**UNC SCHOOL OF MEDICINE
CURRICULUM VITAE**

Personal Information

Name: Daniel Lyle Clarke-Pearson, M.D.

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Education and Training

Fellow	Duke University Medical Center	1979-1981	Gynecology Oncology
Residency	Duke University Medical Center	1975-1979	Obstetrics and Gynecology
Medical Degree	Case Western Reserve University School of Medicine	1971-1975	Medicine
Bachelor of Arts	Harvard College	1966-1970	Biology

Professional Experience

Active Consulting Staff	The Outer Banks Hospital	Oct 2009 – present	Medicine/Oncology Section
Chairman	University of North Carolina at Chapel Hill School of Medicine	September 2005 - present	Obstetrics and Gynecology
Robert A. Ross Distinguished Professor	University of North Carolina at Chapel Hill School of Medicine	September 2005 - present	Obstetrics and Gynecology
James M. Ingram Professor of Gynecologic Oncology	Duke University Medical Center	July 1993-2005	Gynecologic Oncology
Division Director	Duke University Medical Center	July 1987-2005	Gynecologic Oncology
Professor	Duke University Medical Center	July 1987-2005	Obstetrics and Gynecology

Director of Gynecology and Gynecologic Oncology	University of Illinois at Chicago	January 1985-1986	Obstetrics and Gynecology
Associate Professor	University of Illinois at Chicago	July 1984-1986	Obstetrics and Gynecology
Director of Gynecologic Oncology	University of Illinois at Chicago	July 1984-1985	Obstetrics and Gynecology
Associate Professor	Duke University Medical Center	January 1984	Obstetrics and Gynecology
Co-Director, Trophoblastic Disease Center	Duke University Medical Center	July 1982-1984	Obstetrics and Gynecology
Assistant Professor	Duke University Medical Center	July 1980-1984	Obstetrics and Gynecology

Honors and Awards

2009-2010	President, Society of Gynecologic Oncologists
2001-2013	America's Top Doctors for Women (176 Physicians): Women's Health
2008	CREOG National Faculty Award for Excellence in Resident Education
2004	Invited Panel Member, International Consensus Conference of the Prevention of Venous Thromboembolism, Windsor, England
2002	ACOG Roy Pitkin/Elsevier Award: One of top four papers published annually in <u>Obstetrics and Gynecology</u>
2001	America's Top Doctors for Women: Women's Health
1991	Invited Panel Participant, Consensus Meeting on the Prevention of Thromboembolism - Windsor, England
1985	Clinical Research Prize Paper – ACOG District Meeting
1981-1984	Junior Faculty Clinical Fellowship – American Cancer Society
1982	Donald F. Richardson Memorial Prize Paper -Best research paper presented by a Junior Fellow at a District ACOG Meeting
1981	Clinical Research Paper, Second Place ACOG Annual Clinical Meeting
1981	Junior Fellow First Prize Paper – ACOG District IV
1980	American Cancer Society Clinical Fellow

1979

Junior Fellow First Prize Paper – ACOG District IV

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Original Research

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15. Creasman WT, **Clarke-Pearson DL**, Ashe CA, Weed JC Jr: The abnormal pap smear: What to do next. Cancer 48:515, 1981.

ACOG Committee Opinions published during tenure as Committee Chair:

1. Performance enhancing anabolic steroid abuse in women. Committee Opinion No. 484. American College of Obstetricians and Gynecologists. Obstet Gynecol 2011;117:1016–18.
2. Understanding and using the U.S. Medical Eligibility Criteria for Contraceptive Use, 2010. Committee Opinion No. 505. American College of Obstetricians and Gynecologists. Obstet Gynecol 2011;118:754–60.
3. Expedited partner therapy in the management of gonorrhea and chlamydia by obstetrician–gynecologists. Committee Opinion No. 506. American College of Obstetricians and Gynecologists. Obstet Gynecol 2011;118:761–6.
4. Management of vulvar intraepithelial neoplasia. Committee Opinion No. 509. American College of Obstetricians and Gynecologists. Obstet Gynecol 2011;118:1192–4.
5. Vaginal placement of synthetic mesh for pelvic organ prolapse. Committee Opinion No. 513. American College of Obstetricians and Gynecologists. Obstet Gynecol 2011;118:1459–64.
6. Compounded bioidentical menopausal hormone therapy. Committee Opinion No. 532. American College of Obstetricians and Gynecologists. Obstet Gynecol 2012;120:411–5.
7. Well-woman visit. Committee Opinion No. 534. American College of Obstetricians and Gynecologists. Obstet Gynecol 2012;120:421–4.
8. Reprocessed single-use devices. Committee Opinion No. 537. American College of Obstetricians and Gynecologists. Obstet Gynecol 2012;120:974–6.
9. Risk of venous thromboembolism among users of drospirenone-containing oral contraceptive pills. Committee Opinion No. 540. American College of Obstetricians and Gynecologists. Obstet Gynecol 2012;120:1239–42.
10. Over-the-counter access to oral contraceptives. Committee Opinion No. 544. American College of Obstetricians and Gynecologists. Obstet Gynecol 2012;120:1527–31.
11. Postmenopausal estrogen therapy: route of administration and risk of venous thromboembolism. Committee Opinion No. 556. American College of Obstetricians and Gynecologists. Obstet Gynecol 2013;121:887–90.
12. Management of acute abnormal uterine bleeding in nonpregnant reproductive-aged women. Committee Opinion No. 557. American College of Obstetricians and Gynecologists. Obstet Gynecol 2013;121:891–6.
13. Integrating immunizations into practice. Committee Opinion No. 558. American College of Obstetricians and Gynecologists. Obstet Gynecol 2013;121:897–903.

Developed during tenure as Committee Chair:

1. Female age-related fertility decline. Committee Opinion No. 589. American College of Obstetricians and Gynecologists. Obstet Gynecol 2014;123:719–21.

2. Hormone therapy and heart disease. Committee Opinion No. 565. American College of Obstetricians and Gynecologists. Obstet Gynecol 2013;121:1407–10.
3. Professional liability and gynecology-only practice. Committee Opinion No. 567. American College of Obstetricians and Gynecologists. Obstet Gynecol 2013;122:186.
4. Solutions for surgical preparation of the vagina. Committee Opinion No. 571. American College of Obstetricians and Gynecologists. Obstet Gynecol 2013;122:718–20.
5. Understanding and using the U.S. Selected Practice Recommendations for Contraceptive Use, 2013. Committee Opinion No. 577. American College of Obstetricians and Gynecologists. Obstet Gynecol 2013;122:1132–3.
6. Von Willebrand disease in women. Committee Opinion No. 580. American College of Obstetricians and Gynecologists. Obstet Gynecol 2013;122:1368–73.
7. Addressing health risks of noncoital sexual activity. Committee Opinion No. 582. American College of Obstetricians and Gynecologists. Obstet Gynecol 2013;122:1378–83.

Editorials and Letters

1. Clarke-Pearson DL, Geller EJ. Complications of Hysterectomy. Obstet Gynecol 2013; 121:1-21.
2. Clarke-Pearson DL. Thromboprophylaxis in Gynecologic Surgery: Why are we Stuck in 1975? Obstet Gynecol 2011; 118: 973.
3. Martino M, Rajaram L, Maxwell GL, **Clarke-Pearson DL**. Combination Prophylaxis for Thromboembolism Prevention among Gynecologic Oncology Patients Perioperatively. (Letter) Gynecol Oncol 2008; 109: 426-27.
4. **Clarke-Pearson DL**: Prevention of venous thrombosis following gynecologic Surgery. J Gynecol Tech 1(1):11-17, 1995.
5. **Clarke-Pearson DL**: Crafting the operative note: techniques critical to success (editorial). J Gynecol Tech 1(3):119-120, 1995.
6. **Clarke-Pearson, DL**: Reassessment of ovarian cancer: What are our goals? Gynecol Oncol 52:151-153, 1994.
7. Soper JT, **Clarke-Pearson DL**, Berchuck A: The clinical significance of blood transfusion at the time of radical hysterectomy. (Letter). Obstet Gynecol 77:165, 1991.
8. **Clarke-Pearson DL**: The importance of calf vein thrombosis. N Eng J Med 302:752, 1980.

Published Abstracts

1. Barber EL, **Clarke-Pearson DL**. Risk of venous thromboembolism in minimally invasive versus open hysterectomy for endometrial cancer. SGO Annual Meeting 2016.
2. Barber EL, Gehrig PA, **Clarke-Pearson DL**. A risk assessment score for postoperative VTE

among patients undergoing minimally invasive surgery for gynecologic cancer. SGO Annual Meeting 2016.

3. Barber EL, **Clarke-Pearson DL**. Validity of currently available venous thromboembolism risk scores among gynecologic oncology patients.
4. Look K, Brunetto VL, **Clarke-Pearson DL**, Averette H, Major FJ, Alvarez RD, Homesley HD, Zaino R: An analysis of cell type in patients with surgically stages stage IB carcinoma of the cervix: A Gynecologic Oncology Group (GOG) Study. Abstract. Gynecol Oncol 60:117, 1996.
5. Omura GA, Blessing J, Vaccarello L, Berman M, Mutch D, **Clarke-Pearson DL**, Anderson B: A randomized trial of Cisplatin versus Cisplatin + Mitolactol versus Cisplatin + Ifosfamide in advanced squamous carcinoma of the cervix by the Gynecologic Oncology Group (GOG). Abstract. Gynecol Oncol 60:120, 1996.
6. Omura GA, Blessing J, Vaccarello L, Berman M, Mutch D, **Clarke-Pearson DL**, Anderson B: A randomized trial of Cisplatin versus Cisplatin + Mitolactol versus Cisplatin + Ifosfamide in advanced squamous carcinoma of the cervix by the Gynecologic Oncology Group (GOG). Abstract. ASCO, 1995.
7. Alberts DS, Liu PY, Hannigan EV, O'Toole R, Williams SD, Vogel S, Franklin FW, **Clarke-Pearson DL**, Malviya VK, Dubeshter B, Hoskins W, Adelson M, Alvarez RD, O'Sullivan J, Garcia DJ, Sparks D, Rothenberg ML: Phase III study of intraperitoneal (IP) Cisplatin CDDP/Intravenous (IV) Cyclophosphamide (CPA) vs. IV CDDP/IV CPA in patients (Pts) with optimal disease stage III ovarian cancer: A SWOG-GOG Intergroup Study. Abstract. ASCO, 1995.
8. Stehman FB, Bundy BN, Ball H, **Clarke-Pearson DL**: Sites of failure and times to failure in carcinoma of the vulva treated conservatively: A Gynecologic Oncology Group Study. Abstract. AGOS 1995.
9. Omura GA, Blessing J, Vaccarello L, Berman M, Mutch D, **Clarke-Pearson D**, Anderson B: A randomized trial of cisplatin versus cisplatin + mitolactol (CM) versus cisplatin + ifosfamide (CIFX) in advanced squamous carcinoma of the cervix (SCC) by the Gynecologic Oncology Group (GOG). Presented at the 1995 American Society of Clinical Oncology Annual Meeting.
10. **Clarke-Pearson DL**, Berchuck A, Kohler M, Rodriguez GC: Retroperitoneal drains/morbidity of nodes. Society of Gynecologic Oncologists, 1993.
11. Hoskins WJ, McGuire WP, Brady MS, Copeland L, Homesley HD, **Clarke-Pearson DL**: Serum CA-125 for prediction of progression in advanced epithelial ovarian carcinoma (AOC). The Gynecologic Oncology Group (GOG). Proc ASOC (Abstract #707) 11:223, March 1992.
12. McGuire WP, Hoskins WJ, Brady MF, Homesley HD, **Clarke-Pearson DL**: A Phase III trial of dose intensive (DI) cisplatin (CDDP) and Cytosan (CTX) in advanced ovarian cancer (AOC). Proc ASCO, March 1992.
13. Hoskins WJ, McGuire WP, Brady MS, Homesley HD, **Clarke-Pearson DL**: Serum CA-125 for prediction in advanced epithelial ovarian cancer (AOC). The Gynecologic Oncology Group (GOG). Third Meeting of the International Gynecologic Cancer Society, September 22-26, 1991, Cairns, Australia.
14. McGuire WP, Hoskins WJ, Brady MS, Homesley HD, **Clarke-Pearson DL**: A Phase II trial of dose intense (DI) versus standard dose (SD) Cisplatin (CDDP) and Cytosan (CTX) in advanced ovarian cancer (AOC). The Gynecologic Oncology Group (GOG). Third Meeting of the International Gynecologic Cancer Society, September 22-26, 1991, Cairns, Australia.

15. Shpall E, **Clarke-Pearson DL**, Soper JT, Berchuck A, Jones R, Bast R, Lider Y, Vanacek K, Tyler T, Peters W: High dose alkylating agent chemotherapy with autologous bone marrow support in patients with Stage III/IV epithelial ovarian cancer. Society of Gynecologic Oncologists, 1990.
16. Soisson AP, Soper JT, Berchuck A, Creasman WT, **Clarke-Pearson DL**: The role of radiation therapy following radical hysterectomy for carcinoma of the cervix. Society of Gynecologic Oncologists, 1989.
17. Berchuck A, Soisson AP, Soper JT, **Clarke-Pearson DL**, McCarty KS Jr, Bast RC Jr: Cellular expression of CA-125 and metastatic potential of endometrial adenocarcinoma. Society of Gynecologic Oncologists, 1989.
18. Soisson AP, Berchuck A, Soper JT, **Clarke-Pearson DL**, Flowers J, Kinney R, McCarty KS Jr, Bast RC Jr: TAG-72 expression in benign and malignant endometrium. American College of Obstetricians and Gynecologists, Armed Forces District Meeting, 1988.
19. Christensen C, McCarty KS Jr, Flowers J, Soper JT, McCarty KS Sr, **Clarke-Pearson DL**: Progesterone receptor in ovarian carcinoma: Comparison of biochemical and immunohistochemical techniques. American College of Obstetricians and Gynecologists, Annual Clinical Meeting, 1988.
20. Genkins SM, Sotsman HD, Spritzer CE, Herfkens RJ, Carroll BA, Kadir S, **Clarke-Pearson DL**, Coleman RE: Diagnosis of deep venous thrombosis: Comparison of venography with four noninvasive techniques. The Radiological Society of North America, 1988.
21. Mutch DG, Soper JT, Babcock CJ, Christensen CW, **Clarke-Pearson DL**, Hammond CB: Recurrent gestational neoplasia: Experience of the Southeastern Trophoblastic Disease Center. Abstract, Gynecol Oncol 29:133, 1988.
22. Christensen C, McCarty KS Jr, Flowers J, Soper JT, McCarty KS Sr, **Clarke-Pearson DL**: Analysis of estrogen receptor in ovarian carcinoma using biochemical and monoclonal antibody assays. Presented at American College of Obstetricians and Gynecologists District IV Meeting. Atlanta, Georgia, October 1987.
23. **Clarke-Pearson DL**, Creasman WT: Prevention of postoperative deep venous thrombosis by two intense low-dose heparin regimens: A controlled trial. Abstract, Society of Pelvic Surgeons, 1986.
24. **Clarke-Pearson DL**, DeLong ER, Synan IS, Coleman RE, Creasman WT: Variables associated with postoperative deep venous thrombosis. Abstract, Society of Gynecologic Investigation, p. 119, 1986.
25. Siegel RS, Kessler CM, **Clarke-Pearson DL**, Barth S, Fortune W, Reba R, Coleman RE: Application of Indium-111-labeled donor platelets to detection of deep venous thrombosis. Clin Res 32:323A, 1984.
26. Creasman WT, Henderson D, **Clarke-Pearson DL**: Use of estrogens after treatment for adenocarcinoma of the endometrium. Gynecol Oncol 17:2, p. 255, 1984.
27. Siegel RS, **Clarke-Pearson DL**, Barth S, Fortune W, Lewis RJ, Reba R, Coleman RE: Application of Indium-111-labeled donor platelets to detection of deep venous thrombosis and monitoring clot resolution on streptokinase therapy. Blood, Suppl 62:310, 1983.
28. Siegel RS, **Clarke-Pearson DL**, Coleman RE: Indium-111-labeled platelets in the detection of deep venous thrombosis and pulmonary embolism. Blood 50:223, 1982.

29. Postoperative thromboembolism prophylaxis in gynecologic oncology: A prospective, controlled trial of low-dose heparin and external pneumatic calf compression. *Gynecol Oncol*, 1982.

Un-refereed Publications

1. **Clarke-Pearson DL**. Prevention and Management of Venous Thromboembolism (15 minute Video) for the Globathon to End Women's Cancer. September 2014.
2. **Clarke-Pearson DL, Brincat C, Tang J**. Prevention and Management of Venous Thromboembolism in Gynecologic Surgery. *ACOG Update*. Vol 37, No 2. August, 2011.
3. **Clarke-Pearson DL**. Preventing Venous Thromboembolism: Evidence-based Perioperative tactics. *OBG Management*. 2006, 18:56-66.
4. **Clarke-Pearson DL**: Prevention of venous thrombosis following gynecologic surgery in menopausal patients. *Menopausal Medicine* Vol 4 (4):6-9, 1996.
5. Rodriguez GC, **Clarke-Pearson DL**: What is the appropriate preoperative and prenatal screen for hemostatic disorders? *Obstet Gynecol Forum*, November 1991.
6. **Clarke-Pearson DL**, Hume RF: Venous thromboembolic disease in obstetrics and gynecology: Prevention, diagnosis and treatment. *Curr Problems in Obstet Gynecol*, 1989.
7. Hunter VJ, Christensen C, **Clarke-Pearson DL**: Evaluation and management of the abnormal Papanicolaou smear. *North Carolina Family Physician*, 1989.
8. **Clarke-Pearson DL**, Krumholz AB: When the pap smear is equivocal. *Patient Care* 23:43-47, 1989.
9. **Clarke-Pearson D**, DiSaia P, Mastroianni L, Richart R, Weingold AB: Advances in managing endometrial carcinoma. *Patient Care* 22:102-116, 1988.
10. Creasman WT, Smith EB, **Clarke-Pearson DL**: Current concepts of gestational trophoblastic disease. *Female Patient*, 1984.
11. Creasman WT, **Clarke-Pearson DL**: Abnormal cervical cytology: Spotting it, treating it. *Contemporary Obstet Gynecol* 21:53-76, 1983.
12. Hammond CB, **Clarke-Pearson DL**, Soper JT: Management of patients with gestational trophoblastic neoplasia: Experience of the Southeastern Regional Center. In: *The Proceedings of the World Congress on Gestational Trophoblastic Neoplasia*, Nigeria, 1982.
13. **Clarke-Pearson DL**: Application of impedance phlebography in obstetrics. Symposium on Noninvasive Diagnostic Techniques in Vascular Disease. San Diego, California, 1979.
14. **Clarke-Pearson DL**: The O.S.R. as an influence to health education. *The Scalpel*, Journal of Alpha Delta Alpha Medical Honor Society, 1975.

Teaching Record

2018

Visiting Professor, University of West Virginia, Morganton, WV

Antonio Palladino Lectureship

2016 Plenary Session, Society of Pelvic Surgeons, St Louis, Mo. "Venous Thromboembolism in

- Minimally Invasive Compared with Open Hysterectomy for Endometrial Cancer”
- Key Note Speaker. ACOG Armed Forces District Meeting, Orlando, FL
- Visiting Professor and Research Day Judge, Cleveland Clinic Department of Obstetrics and Gynecology and Women’s Research Institute, Cleveland, Ohio
- Visiting Professor, Department of Obstetrics and Gynecology, Carilion Roanoke Memorial Hospital, Roanoke, Va.
- 2015** Visiting Professor
University of Michigan
- 2014** Visiting Professor
Massachusetts General Hospital, ObGyn Department Grand Rounds
Boston, MA
Invited speaker: ACOG District II Annual Meeting, New York City
“Uterine Morcellation: A Decision Analysis”
- 2013** Visiting Professor and Resident Research Day Judge
Department of Obstetrics and Gynecology, University of Nebraska
Omaha, NE
Visiting Professor, Emory University Department of Obstetrics and Gynecology
Atlanta, GA
- Key Note Speaker: Inaugural Ireland Ovarian Cancer Forum
“Surgery for Ovarian Cancer”
Dublin, Ireland
Panel Moderator, American College of Surgeons Annual Clinical Congress
“General Surgery in the Pregnant Patient”
Washington, DC
- 2012** Clifford Wheelless Lecture, Johns Hopkins University, Department of Obstetrics and Gynecology,
Baltimore, MD
- Panel Moderator, American College of Surgeons Annual Clinical Congress
“Multidisciplinary approach to Vaginal Fistula”
Chicago, IL
- Resident Research Day Judge and Visiting Professor
Department of Obstetrics and Gynecology, Greenville Hospital System, Greenville, SC
- Visiting Professor: University Teaching Hospital, Department of Obstetrics and Gynecology,
Lusaka, Zambia
Cervical Cancer management
Current Treatment of Vulvar Carcinoma
Visiting Professor: Center for Infectious Disease Research in Zambia (CIDRZ), Lusaka, Zambia
Human Papilloma Vaccine for the Prevention of Cervical Cancer
- Visiting Professor: Inova Fairfax Hospital Women’s Center, Fairfax VA
- Visiting Professor: Emory University School of Medicine, Department of Obstetrics and
Gynecology. Atlanta, GA
- 2011** Sloane Symposium: Current Issues and Controversies in Obstetrics and Gynecology
Columbia University, College of Physicians and Surgeons, Department of Obstetrics and

Gynecology

Vandewiele Lecturer: "Prevention of Venous Thromboembolism in Gynecologic Surgery"

Guest Lecturer and Judge: Resident Research Day, Columbia University
"What to say in your Operative Note"

University of Kentucky: Residents' Research Day Speaker

Virginia Commonwealth University School of Medicine
Department of Obstetrics and Gynecology Annual Ware-Dunn Symposium
Keynote speaker

2010 New England Obstetrical and Gynecological Society, Sturbridge, MA
Invited Speaker

ACOG Annual Clinical Meeting, San Francisco, CA
Luncheon Seminar Leader

George Washington University Medical Oncology Review Course
Washington, DC
Invited Faculty

MD Anderson Cancer Center Medical Oncology Review Course
Houston, TX
Invited Faculty

The Society of Gynecologic Oncology of Canada
Royal College of Physicians and Surgeons of Canada
Annual Meeting
Invited Lecturer: Thromboprophylaxis in Minimally Invasive Surgery

Visiting Professor
University of South Florida, Tampa, FL
Resident Research Day

2009 ACOG District IV Meeting, Asheville, NC
"Prevention of Venous Thromboembolism"
"Stump the Professors: Panel"

American College of Surgeons' Annual Meeting, Chicago, IL
"Complicated Hysterectomy"

Visiting Professor: Hartford Hospital, Hartford CT

Visiting Professor: University of Connecticut, Farmington, CT

Visiting Professor: Memorial Sloan Kettering Cancer Center

Southern Obstetric and Gynecologic Seminar, Asheville, NC
"Prevention of VTE following Gynecologic Surgery"
"The Operative Note: What to say?"

Woman's Hospital 7th Annual Founders Commemorative Lectureship, Woman's Hospital, Baton Rouge, LA

2008 Visiting Professor, Department of Obstetrics and Gynecology, Yale University

Course Director, ACOG CME Course “Complex Pelvic Surgery”, Phoenix, AZ

Invited Speaker: First Annual Gynecologic Cancer Symposium, Washington, DC April 18, 2008

Visiting Professor, University of Wisconsin Resident’s Research Day, Ben M. Peckman Memorial
Lecturer, Madison, WI

ACOG representative to Symposium on Surveillance for Venous Thrombosis,
American Society of Hematology, Washington DC

2007 Visiting Professor, Department of Obstetrics and Gynecology, University of Miami

Faculty, University of Utah CME Course “Obstetrics and Gynecology: Update and Current
Controversies” Park City Utah

Visiting Professor, Department of Obstetrics and Gynecology St. Louis University, St. Louis MO

Invited Lecturer: Marvin Camel Memorial Lecture, Washington University, Department of
Obstetrics and Gynecology, St Louis, MO

Presidential Panel Speaker: Society of Pelvic Surgeons Annual Meeting, Cleveland, OH “What
Can We do to prevent Venous Thromboembolism?”

2006 Course Director: ACOG Annual Clinical Meeting: “Complex Gynecologic Surgery, Washington
DC

Invited Speaker, ACOG District IV Annual Meeting, Palm Beach, FL

2005 Course Director: ACOG Annual Clinical Meeting: “Complex Gynecologic Surgery, San
Francisco

Course Director: ACOG Free-standing CME Course “Complex Gynecologic Surgery, Preventing
Complications” Dana Point, CA

2004 Society of Surgical Oncology: Symposium on Prevention of Venous Thromboembolism in the
Surgical Oncology Patient

Postgraduate Course Faculty: ACOG Cancun, Mexico “Advanced Gynecologic Surgery”

American College of Obstetricians and Gynecologists, Annual Clinical Meeting, Philadelphia, PA
Faculty, 120 Course: Special Topics for the Advanced Gynecologic Surgeon
Faculty, Luncheon Seminar: “Prevention of Postoperative Venous Thromboembolism”
Speaker: “Late-breaking News in Gynecologic Oncology”

Visiting Professor, University of Kansas School of Medicine, Truman Medical Center

Faculty: ACOG Indiana Section Meeting, Indianapolis
“Surgery in the Obese Patient”, “Surgical Instruments”

2003 Faculty, The 3rd Annual Cancer Conference, Aultman Cancer Center, Canton Ohio
“Prevention and Management of Perioperative Venous Thromboembolism in the
Gynecologic Cancer Patient”

Visiting Professor, Department of Obstetrics and Gynecology, University of Massachusetts,
Worcester, MA

- 2002** Visiting Professor
Bowman Gray School of Medicine
- Residents' Day Research Judge
Winston Salem, NC
- American College of Surgeons' Annual Clinical Congress
Panel Discussant: "Surgical Problems: Unexpected adnexal mass, tuboovarian abscess"
Video Presentation: "Intraoperative Radiation Therapy for the treatment of Recurrent Cervical Carcinoma"
Discussant: Video Presentation "Laparoscopic Infrarenal paraaortic lymphadenectomy"
- 2001** ACOG Annual Meeting
Postgraduate Seminar
Gynecologic Surgery in the Elderly
- Visiting Professor
University of West Virginia, Faculty, Cancer Center Annual Symposium
"Chemosensitization and Radiation Therapy in the treatment of locally advanced cervical carcinoma."
- 2000** Keynote Speaker
Knoxville Obstetrical and Gynecological Society
- ACOG Annual Meeting (Course Director)
Postgraduate Course
Gynecologic Surgery for the Advanced Pelvic Surgeon
- Visiting Professor
East Carolina University School of Medicine
- Visiting Professor
Pennsylvania State University School of Medicine (Hershey)
- George Washington University
Medical Oncology Board Review Course (Faculty)
- 1999** ACOG Annual Meeting (Course Director)
Postgraduate Course
Gynecologic Surgery for the Advanced Pelvic Surgeon
- George Washington University School of Medicine
Medical Oncology Board Review Course (Faculty)
- Visiting Professor
University of Virginia Health Sciences Center
- ACOG Annual Meeting (Course Director)
Postgraduate Course
Gynecologic Surgery for the Advanced Pelvic Surgeon
- 1998** ACOG Annual Meeting (Course Director)
Postgraduate Course
Gynecologic Surgery for the Advanced Pelvic Surgeon

George Washington University School of Medicine
Medical Oncology Board Review Course (Faculty)

Visiting Professor
Temple University School of Medicine

Keynote Speaker
Maryland Obstetrical and Gynecological Society

Visiting Professor
University of Louisville
“Prevention of Postoperative Venous Thromboembolism”
“Management of Patients with Thrombophilias”

1997 Visiting Professor
University of Utah, Salt Lake City

ACOG Annual Meeting (Course Director)
Postgraduate Course
Advanced Surgery for the Gynecologist

Visiting Professor
Cleveland Clinic Foundation
Department of Obstetrics and Gynecology
Cleveland, Ohio

George Washington University School of Medicine
Medical Oncology Board Review Course (Faculty)

Keynote Speaker
Chicago Gynecological Society

Visiting Professor
University of Louisville School of Medicine

Visiting Professor
Washington University School of Medicine

Visiting Professor
Johns Hopkins University School of Medicine

ACOG Annual Clinical Meeting
Faculty, 120 Course: Special Topics for the Advanced Gynecologic Surgeon
Faculty, Seminar: “Gynecologic Surgery in the Elderly”
Faculty, Luncheon Seminar: “Prevention of Postoperative Venous Thromboembolism”

American College of Surgeons’ Annual Clinical Congress
Panel Discussant: “Management of Gynecologic Problems Encountered by the General Surgeon at the time of Surgery. “Surgical Management of Ovarian Cancer Discovered at the time of Laparotomy”

1996 Visiting Professor
Dartmouth Medical School

Director ACOG Postgraduate Course
Annual Clinical Meeting

Special Problems for the Advanced Gynecologic Surgeon

Visiting Professor
University of Tennessee School of Medicine
Chattanooga, Tennessee

Visiting Professor
University of South Florida School of Medicine
Tampa, Florida

Visiting Professor
Washington University School of Medicine
St. Louis, Missouri

John L. McKelvey Lecturer
New Treatments for Ovarian Cancer
University of Minnesota
Minneapolis, Minnesota

Faculty - Taubman Ovarian Cancer Symposium
St. Joseph's Hospital
Tulsa, Oklahoma

ACOG Postgraduate Course (Course Director)
San Juan, Puerto Rico
Advanced Pelvic Surgery

1994 ACOG Clinical Meeting CME Course
Orlando, FL
"Gynecologic Cancer"

Guest Speaker
Seattle Gynecological Society Assembly

1993 Visiting Professor - Department of OB/GYN
University of Massachusetts
Worcester, Massachusetts

ACOG Clinical Meeting - CME Course
Washington, DC
"Gynecologic Surgery"

PostGraduate Course in Obstetrics and Gynecology
Kaiser-Permanente - Maui, Hawaii
"Screening for Ovarian Cancer"
"Management of CIN with LEEP"
"Difficult Vaginal Hysterectomy"
"Incisions and Wound Closures"

Duke/US Surgical Course
"Laparoscopic Assisted Difficult Hysterectomy"

Visiting Professor - Mt. Sinai Hospital
Baltimore, MD
"Prevention of Thromboembolism"
"Management of Ovarian Cancer"

- 1992** Visiting Professor - Department of OB/GYN
University of Massachusetts
Worcester, Massachusetts
- 1991** Visiting Professor
George Washington University School of Medicine
- Course Director - ACOG Course (120 series)
Annual Clinical Meeting
New Orleans, Louisiana
"Gynecologic Oncology for the Practicing Gynecologist"
- Course Director - ACOG Course
Vancouver, British Columbia, Canada
"Gynecologic Surgery"
- Visiting Professor
Florida Hospital Cancer Center
Orlando, Florida
- Paper Presentation
Poster Presentation
Society of Gynecologic Oncologists
Orlando, Florida
- Visiting Professor
Ohio State University School of Medicine
Columbus, Ohio
- Medical Oncology Board Review Course
George Washington University
Washington, DC
"Cervical, Vulvar and Vaginal Cancer"
"Gestational Trophoblastic Disease"
- 1990** Society of Gynecologic Oncologists
Breakfast Seminar
"Diagnosis and Prevention of Postoperative Venous Thrombosis"
- Course Director - ACOG Course (120 Series)
Annual Clinical Meeting
San Francisco, California
"Update in Clinical Gynecologic Oncology"
- Seminar, ACOG Clinical Meeting
"Prevention of Postoperative Venous Thrombosis"
- 1989** Tumor Conference, Moore Regional Hospital
Pinehurst, North Carolina
- Course Director - ACOG Course (120 Series) Annual Clinical Meeting, Atlanta, Georgia
"Update in Clinical Gynecologic Oncology"
- Seminar, ACOG Clinical Meeting
"Management of Early Ovarian Cancer"

Luncheon Conference, ACOG Annual Meeting
"Reproductive Outcome Following Cancer Treatment"

Medical Oncology Board Review Course, George Washington University, Washington, DC
"Cervical Cancer"

1988 Matt Weiss Symposium
St. Louis, Missouri

ACOG Annual Clinical Meeting
Poster Session Presentation
Review of Clinical Research Paper
Review of Surgical Film
Clinical Seminar Presentation

ACOG Course
Juneau, Alaska
"Gynecologic Surgery"

1987 Update in Obstetrics and Gynecology
Williamsburg, Virginia

North Carolina Obstetrical and Gynecological
Society Meeting, Southern Pines, North Carolina

Visiting Professor, University of Minnesota School of Medicine, Minneapolis, Minnesota

ACOG Annual Clinical Meeting
Clinical Paper Presentation
Clinical Seminar Presentation

Southern Obstetrics and Gynecology Seminar
Asheville, North Carolina

Satellite Teleconference
Chicago, Illinois
"Selected aspects of the care of the menopausal woman"

Chicago Medical Schools' Review Course
Chicago, Illinois
"Endometrial Carcinoma"

Smokey Mountain Obstetric and Gynecologic Seminar, East Tennessee State University
Johnson City, Tennessee

Grants

Active Grants:					
None at this time					
Completed Grants:					

Project Period	Agency	Title	Amount	Role	% of Effort
9/27/05-3/10/10	NIH/NICHD	Women's Reproductive Health Research (WRHR) Career Development Center at UNC - HDD050113-02	\$370,367 Annual Direct Costs	Principal Investigator	
3/1/00-3/31/02	Pharmacia Upjohn Pharmaceuticals	Randomized Comparison of Low Molecular Weight Heparin vs. Oral Anticoagulant Therapy for Long Term Anticoagulation in cancer patients – 98-Frag-069	\$ 73,000	Principal Investigator	
1/1/99-6/15/00	Zeneca Pharmaceuticals, Inc	Phase II/III Trial of IV ZD9331 in patients with recurrent refractory ovarian cancer	\$ 18,320	Principal Investigator	
6/1/98-6/1/00	Pharmacia Upjohn Pharmaceuticals	Prospective Randomized Trial Comparing Pneumatic Compression stockings To Low Molecular Weight Heparin (dalteparin) in the prevention of postoperative venous Thrombosis	\$ 100,760	Principal Investigator	
06/01/95 - 05/31/2000	National Cancer Institute	Hyperthermia and Perfusion Effects in Cancer Therapy	\$10,930,969	Investigator	2%
03/15/98-03/14/00	Novartis Pharmaceuticals	PSC 833 with taxol and carboplatin vs. carboplatin alone in patients with stage III ovarian cancer	\$ 102,240	Principal Investigator	
8/1/97-7/31/99	NIH	Hyperthermia and Perfusion Effects in Cancer Therapy	\$ 1,832,501	Co-Investigator	
5/28/97-12/31/98	Smithkline Beecham Pharmaceuticals	Oral Topotecan Single Agent for 5 days in patients with ovarian cancer	\$ 81,600	Principal Investigator	
01/01/93-12/31/98	National Cancer Institute	Comprehensive Cancer Center Core Support Grant	\$ 4,442,597	Program Director	10%
06/01/94 -	National Cancer	Autologous Bone	\$641,613	Investigator	10%

03/31/97	Institute	Marrow Transplantation in Breast and Ovarian Cancer: Project IB			
03/15/96-05/30/96	Ethicon, Inc	An Open, Controlled, Rand, Multicenter, Evaluation of Dyed Monocryl (Poliglecaprone 25) Synthetic Absorbable Suture as Compared to Surgical Gut (Chromic) Absorbable Suture	\$ 4,000	Principal Investigator	
1987-1996	American Cancer Society	Clinical Oncology Fellowship	\$ 20,000 (Direct)	Principal Investigator	5%
10/01/92-09/30/94	Centocor, Inc.	CA125 Post-Market Evaluation	\$ 8,750	Principal Investigator	5%
12/15/93-09/21/94	Smith-Kline Beecham Pharmaceutical	Phase III Topotecan versus Taxol in Women with Advanced Ovarian Carcinoma	\$ 37,500	Principal Investigator	5%
12/15/93-08/14/94	Smith-Kline Beecham Pharmaceutical	II Topotecan, Given as Five Daily Doses Every 21 Days in Ovarian Cancer	\$ 37,500	Principal Investigator	10%
07/01/89 - 03/31/94	Gynecologic Oncology Group	Gynecologic Oncology Group, Duke University Medical Center	\$ Contingent on number of patients	Co-Principal Investigator	30%
01/01/91 – 09/01/93	Organon, Inc.	ORG 2766 as a Neuroprotector from Cisplatin Chemotherapy for Ovarian Cancer	\$97, 575	Principal Investigator	10%
02/01/91 - 01/31/92	Organon, Inc.	Decapeptyl Treatment of Advanced Ovarian Cancer (Phase II Trial)	\$100,098	Principal Investigator	10%
11/01/90-10/31/91	Cytogen, Inc.	111In-CYT-103 Oncoprobe Evaluation of Ovarian Cancer	\$ 124,000	Principal Investigator	10%
07/01/86-06/30/91	National Institutes of Health	Avoidable Mortality from Cancers in Black Populations	\$ 4,647,291	Co-Investigator	10%
06/01/87 - 05/31/89	Public Health Service	Improved Instrumentation for the Diagnosis of Venous Thrombosis	\$162,804 (Direct)	Co-Principal Investigator	10%
05/01/88 -	National Cancer	Gynecologic	\$97,073	Co-Principal	10%

04/30/89	Institute	Oncology Group, Duke University Medical Center	(Direct)	Investigator	
01/01/88 - 12/30/88	Centocor, Inc.	Evaluation of the Safety and Preliminary Diagnostic Accuracy of IV Administered Indium-111-labeled OC-125 Monoclonal Antibody in Patients with Carcinoma of the Ovary	\$ 20,000 (Direct)	Co-Principal Investigator	5%
01/01/88 - 12/30/88	Centocor, Inc.	Evaluation of the Safety and Preliminary Diagnostic Accuracy of IV Administered Indium-111-labeled OV-TL3 Monoclonal Antibody in Patients with Carcinoma of the Ovary	\$ 40,000 (Direct)	Co-Principal Investigator	5%
05/01/85- 04/30/87	National Cancer Institute	Illinois Cancer Council - Gynecologic Oncology Group	\$ 21,000 (Direct)	Co-Principal Investigator	10%
07/01/81- 06/30/84	American Cancer Society	Junior Faculty Clinical Fellowship	\$ 35,000	Principal Investigator	30%
01/01/83- 12/31/83	Trent Foundation	In-vitro chemotherapy sensitivity testing of ovarian carcinoma	\$ 1,000	Principal Investigator	5%

PROFESSIONAL SERVICE

To discipline:

A. National/International

- 2018** President, Council of University Chairs of ObGyn (CUCOG)
- 2016** President Elect: Council of University Chairs of ObGyn (CUCOG)
- 2016 Vice President: Bayard Carter Society (Duke University ObGyn Alumni)
- 2016 Member, ACOG Grievance Committee
- 2016 Member, American College of Surgeons, Commission on Cancer
- 2016 American College of Obstetricians and Gynecologists)
- 2016
- 2015** Secretary-Treasurer: Council of University Chairs of ObGyn (CUCOG)
- 2015 American College of Surgeons Board of Governors. ACOG Representative (alternate)

2014

2014 Chair, External Site Visit Committee, Department of Obstetrics and Gynecology, Penn State
2014 University College of Medicine, Department of Obstetrics and Gynecology Member,
CUCOG Executive Board

2011

2011 Member, American College of Surgeons Advisory Committee (ObGyn)
2011 Member, CUCOG Executive Committee
2011 Chair, ACOG Committee on Gynecologic Practice
Chair, SGO Nominating Committee

2010-2013

2010-2013 Immediate Past President, SGO
2010-2013 Member, ACOG Executive Board (Representing the Society of Gynecologic Oncology)
2011-2013 Chair, Committee on Gynecologic Practice, ACOG
2007 -2010 Member, Education/Research Committee, Society of Pelvic Surgeons
1988- 2005 Board Examiner: Obstetrics and Gynecology , ABOG
2010-2011 Vice-Chair, Committee on Gynecologic Practice, ACOG
2010 President, Society of Gynecologic Oncologists
2009-2010 Editorial Board, Precis, Gynecology, ACOG
Program Chair, Society of Pelvic Surgeons

2008

2008-2010 Committee on Gynecologic Practice, ACOG
2008 President Elect II, Society of Gynecologic Oncologists
2008 Chair, Membership Committee. Society of Pelvic Surgeons
2007-2008 Vice President, Society of Gynecologic Oncologists

2007

2007 Editorial Board: Precis, Oncology, ACOG
2007 SGO Executive Council, Society of Gynecologic Oncologists
2007 Chair, Task Force to select Editor and Chief, Gynecologic Oncology, Society of
Gynecologic Oncologists
2007 Co-Chair, Strategic Planning Committee, Society of Gynecologic Oncologists
2007 Member, By-laws Committee, Society of Gynecologic Oncologists

2005

2005 NC Breast and Cervical Cancer Control Program's (BCCCP) Medical Advisory
Committee, North Carolina Department of Environment, Health, and Natural Resources
2005 Member, Clinical Cancer Committee, Moses Cone Health System
2005 Director, Gynecologic Oncology Program, Moses Cone Health System
2005 Member, Cancer Center Executive Committee, Moses Cone Health System
1998-2005 Member, Executive Committee Cancer Center Clinical Service Unit, Duke University
1998-2005 Co-Medical Director, Surgical Oncology Clinic, Duke University
1992-2005 Member, Operating Room Committee, Duke University
1991-2005 Principal Investigator, Duke University, Gynecologic Oncology Group
1987-2005 Director of Gynecologic Oncology Fellowship Program (Duke Univ), ABOG
1987-2005 Director, Gynecologic Oncology Program, Duke Comprehensive Cancer Center, Duke
University
1987-2005 Member, Steering Committee Strategic Planning Task Force, Duke Comprehensive
Cancer Center, Duke University
1987-2005 Member, Executive Committee, Duke Comprehensive Cancer Center, Duke University

2003

2003 Nominating Committee, Society of Gynecologic Oncologists
2003 President and Program Chairman, Mid Atlantic Gynecologic Oncology Society

2002

2002 President-Elect, Mid Atlantic Gynecologic Oncology Society
2002 Member, Membership Committee, Society of Pelvic Surgeons
2002 Member, Oncology Strategic Planning Council, Duke University

2001

2001 Editorial Board: Precis, Oncology, ACOG
2001 Board Examiner: Gynecologic Oncology, ABOG

2000

2000 Member, Nominating Committee (AGOS Foundation)
2000 Program Chairman (Annual Meeting), Mid Atlantic Gynecologic Oncology Society
1994-2000 Member, Education Committee, Society of Gynecologic Oncologists

1999

1996-1999 Member, Fellowship Committee, AGOS

1998

1994-1998 Council Member, Society of Gynecologic Oncologists
1990-1998 Ovarian Cancer Committee, Gynecologic Oncology Group

1997

1993-1997 Editorial Board Member, Duke Cancer Report, Duke University
1993-1997 Committee on Gynecologic Practice, ACOG
1993-1997 Chairman, Committee on Gynecologic Oncology Practice, ACOG
1993-1997 ACOG Liaison Representative to the Society of Gynecologic Oncologists
1994-1997 Member, Committee on Clinical Practice, Society of Gynecologic Oncologists

1995

1994-1995 Chairman, 1995 Program Committee, Society of Gynecologic Oncologists

1994

1993-1994 Ad hoc Council Member, Society of Gynecologic Oncologists
1993-1994 Ad hoc Committee on Clinical Practice Policy Development Society of Gynecologic
Oncologists
1994 Society of Pelvic Surgeons

1993

1991-1993 Chairman, Gynecology Committee, North Carolina OB/GYN Society
1991-1993 Member, Professional Activities Committee, North Carolina OB/GYN Society
1993 Medical Director, Duke North Hospital, 5900 Unit, Duke University
1993 Fellow, American Gynecological and Obstetrical Society
1993 Member, Ad hoc Committee to Define Criteria for Tenure in Clinical Medicine, Duke
University
1993 Department of Surgery Chairman Search Committee, Duke University

1992

1990-1992 Member, Task Force on Cervical Cancer, Chairman, Subcommittee on Impact of
Appropriate Follow-up Care, North Carolina Department of Environment, Health, and
Natural Resources

1991

1987-1991 Co-Principal Investigator, Duke University Grant, Gynecologic Oncology Group
1987-1991 Committee on Technical Bulletins, ACOG
1991 Board Examiner: Gynecologic Oncology, ABOG
1991 Member, Director of Surgical Pathology Search Committee, Duke University

1990

- 1990 Member, Department of Pathology Chairman Search Committee, Duke University
- 1982-1990 Gynecologic Management Committee, Gynecologic Oncology Group

1989

- 1989 Fellow, American College of Surgeons

1988

- 1988 Mid-Atlantic Gynecologic Oncology Society
- 1988 Southern Obstetrical and Gynecological Seminar
- 1988 International Gynecologic Cancer Society
- 1988 Mid-Atlantic Gynecologic Oncology Society
- 1988 Southern Obstetrical and Gynecological Seminar

1987

- 1985-1987 Chicago Medical Society
- 1985-1987 Illinois Cancer Council
- 1985-1987 Illinois State Medical Society
- 1985-1987 Chicago Association of Gynecologic Oncologists
- 1987 North Carolina Medical Society
- 1987 North Carolina Obstetrical and Gynecological Society
- 1987 American Society of Clinical Oncologists

1986

- 1986 Chicago Gynecological Society

1985

- 1982-1985 Co-Principal Investigator, Duke University Grant, Gynecologic Oncology Group
- 1985 Central Association of Obstetricians and Gynecologists
- 1985 Central Association of Obstetricians and Gynecologists
- 1985 American Medical Association

1982

- 1982 Gynecologic Oncology Group
- 1982 Society of Gynecologic Oncologists
- 1982 Fellow, American College of Obstetricians and Gynecologists

1979

- 1979 Piedmont Obstetrical and Gynecological Society
- 1979 Bayard Carter Society of Obstetricians and Gynecologists
- 1979 Junior Fellow Section Chairman, ACOG

1978

- 1978 Junior Fellow Section Co-Chairman, ACOG

1977

- 1977 Junior Fellow Section Program Chairman, ACOG

B. Within UNC-Chapel Hill

- 2018-2021 Member, School of Medicine Promotions and Tenure Committee
- 2013-present Member, UNC Hospitals Committee of Perioperative Leaders
- 2011-present Member, Physicians and Associates Executive Committee
 - Member, P&A Finance and Compensation Committee
 - Member, P&A Committee on Payer Relations

2009-present Member, Strategic Planning Committee: Hillsboro Hospital

2009-present Member, Strategic Planning Committee UNC HCS
2008-present Member, Dean's Advisory Committee on Part-Time Tenure Track Positions
2008-present Member Geographic Strategic Planning Committee
2008-present Member UNC Strategic Planning Committee: Outpatient Surgery
2008-present Member UNC Strategic Planning Committee: Oncology
2007-present Member, Sheps Center Advisory Board
2007-present Member, Center for Women's Health Research Advisory Board
2007-present Team Leader (Attending Physicians' Experience) UNC Hospital Commitment to Caring
2006-present Medical Director, NC Women's Hospital Ambulatory Services
2005-present Dean's Advisory Committee
2005-present UNC Hospital Executive Committee
2005-present Physician and Chief, North Carolina Women's Hospital
2005-present Member, Physician and Associates Board
2005-present Member, UNC Lineberger Cancer Center
2006, 2007 Chair, Data Safety Monitoring Board: An International Multi-Center Phase III Study of
Chemoradiotherapy versus chemoradiotherapy plus hyperthermia for locally advanced
cervical

Editorial Board Member

1994-2004 Postgraduate Obstetrics and Gynecology
2003 Précis, Oncology, Second Edition
1995-2001 Associate Editor, Journal of Gynecologic Techniques
1994-2000 Gynecologic Oncology

Journal Reviewer

Obstetrics and Gynecology
New England Journal of Medicine
American Journal of Obstetrics and Gynecology
Journal of the American Medical Association (JAMA)
Annals of Internal Medicine
Pharmacotherapy
Fertility and Sterility
Gynecologic Oncology
Cancer
International Journal of Gynecology and Obstetrics
Journal of Pelvic Surgery

Exhibit B

- “A Survey of the Long-Term Effects of Talc and Kaolin Pleurodesis.” *British Journal of Diseases of the Chest* 73 (1979): 285–88. [https://doi.org/10.1016/0007-0971\(79\)90054-8](https://doi.org/10.1016/0007-0971(79)90054-8).
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- . "Genital Use of Talc and Risk of Ovarian Cancer: A Meta-Analysis." *European Journal of Cancer Prevention: The Official Journal of the European Cancer Prevention Organisation (ECP)* 27, no. 3 (2018): 248–57. <https://doi.org/10.1097/CEJ.0000000000000340>.
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Exhibit C

DANIEL CLARKE-PEARSON, MD PRIOR TESTIMONY

Rappaport v. Raleigh Ob/Gyn Centre, P.A., et al., No. 14-CVS-1438. Superior Court of North Carolina, Wake County.

Exhibit 6

**UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY**

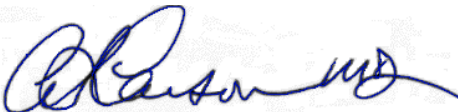
**IN RE JOHNSON & JOHNSON
TALCUM POWDER PRODUCTS
MARKETING, SALES PRACTICES,
AND PRODUCTS LIABILITY
LITIGATION**

MDL NO. 16-2738 (FLW) (LHG)

THIS DOCUMENT RELATES TO ALL CASES

**RULE 26 EXPERT REPORT OF
ARCH CARSON, MD, PHD**

Date: November 16, 2018



Arch Carson, MD, PhD

Talcum Powder and Ovarian Cancer

1. Introduction

I was asked to explain the relationship between the regular perineal use of talc-based personal hygiene products and the subsequent development of ovarian cancer in their users. I intend this report to explain this relationship. I will describe ovarian cancer, what is known about its natural history, and will present statistics regarding its incidence, prevalence and fatality. I will then describe what talc is and why talcum powder is used in personal care products. I will then present the scientific evidence linking talc-based personal hygiene products and their components with cancer, and will show how the various components of this evidence, along with other data, lead me to conclude that regular perineal application of talcum powder products causes ovarian cancer in some users, and raises the risk of ovarian cancer in all users.

2. Qualifications

I am a physician who specializes in the practice of medical toxicology. I am currently an Associate Professor at the University of Texas School of Public Health in Houston and the Program Director of the Occupational and Environmental Medicine Residency training program at the University of Texas Health Science Center at Houston. I received my medical degree from the Ohio State University and a doctor of philosophy degree in Toxicology from the Kettering Laboratory at the University of Cincinnati. I am board certified by the American Board of Preventive Medicine in Occupational Medicine, and have been in the continuous practice of medical toxicology since 1991. My professional activities have included patient care, basic and applied research, teaching of medical students, graduate students and post-graduate medical trainees, and professional consulting. I have been a program director of the NIOSH-funded Education and Research Center at the University of Texas for 19 of the last 21 years. Other major collaborations include as Liaison for the World Health Organization Collaborating Centre in Occupational Health and as environmental exposure consultant to the MD Anderson Cancer Center in Houston. My curriculum vitae is attached to this report as Exhibit A.

3. Information reviewed and methodology employed

In the preparation of this report, I have reviewed relevant published scientific and medical literature, reports and documents produced in the process of litigation, and various other documents and websites that I believed to be pertinent to the refinement or extension of my professional opinions. I applied the same methodology and scientific rigor in this research that I use in my academic and clinical practice. Documents and other sources which I considered in reaching my opinions are listed in Exhibit B, "Materials and Data Considered."

4. What is ovarian cancer?

a. What is cancer?

All types of cancer involve the uncontrolled growth and accumulation or dissemination of cells that originated from normal cells, but have been altered so that they behave differently. The many cells of a single cancer that result from this change are typically all derived from a single progenitor cell, and represent a clone of cells. When this clone

reaches sufficient numbers, the cells themselves may develop into a recognizable “mass” that is called a tumor. Tumors may cause symptoms and other health problems simply by taking up space and putting pressure on neighboring structures or blocking important fluid channels or nerves, thus disrupting normal functions of the body. Still other cancers can proliferate into the blood stream. As the number of cancerous cells increase, the biochemically active substances that they produce can also become a problem resulting in abnormal biological responses throughout the body. Some substances that might become a problem in this way include normal or abnormal hormones, enzymes, antibodies, and proteins. Cancerous cells are considered malignant if they lose their normal tendency to stop proliferating when they have filled a space or the bounds of their particular tissue type, referred to as contact inhibition. Malignant cells ignore these boundary cues and may invade other tissue spaces and organs with devastating results. They may also migrate via the blood stream or other routes to distant sites within the body where they set up a new location of tumor growth and tissue invasion. This process is called metastasis. Typically, cancers are not diagnosed until they produce sufficient symptoms or biochemical abnormalities that lead to an exhaustive diagnostic search resulting in their discovery. Occasionally, cancers are discovered accidentally as part of another investigation, e.g. a chest x-ray may find an asymptomatic lung cancer; a blood test may disclose a telltale abnormality. Still fewer cancers are discovered before they cause health problems through screening tests that are sensitive and specific enough to detect common cancers at a preclinical and hopefully highly treatable stage, e.g. routine colonoscopies to detect colon cancer, or PSA blood tests to detect prostate cancer.

b. Carcinogenesis-a two-step process

The process of normal cells becoming cancer cells is generally recognized as resulting from a two-step process.

Initiation. During initiation, a change is produced at one or more places in the DNA of a cell’s chromosomes. Because the DNA represents the genetic code that becomes duplicated and passed along to cells that arise from it, when that cell divides to produce two cells, the change to the genetic code is also duplicated and is present in both of them.

Normally, the abnormal cell that results from a change in the genetic code cannot survive because its cellular machinery is also abnormal and poorly or non-functional. Less often, if the cell is able to survive in the body, it is still abnormal and deformed, and is recognized by the body’s immune system as alien. The immune system attacks it and destroys it, and it does not survive. In the very rare instance that an alteration to the genetic material results in a survivable hereditary change that is not fatal, and which can escape the surveillance of the body’s immune system, the resulting clone may live and persist. (Coussens LM, 2002)

Promotion - Once a cancer clone has been produced, it is at risk for being discovered and destroyed by the body’s immune system, or failing to thrive in an environment for which it is not suited. Promotion is the process by which the cancer clone is shielded

from the body's defenses and is stimulated to undergo rapid growth, transforming a microscopic cancer clone into a self-sustaining symptomatic cancer over time. (Ferrante D, 2007) (Coussens LM, 2002)

Most known carcinogenesis events occur by the two-step process and involve a long latent period between the moment of the alteration in the genetic material and the recognition that a cancer is present. In human cancers, this latent period is often several months to many years in length. The latency period for ovarian cancer, generally, and for cancers induced by environmental agents is usually quite long, often >20 years. (Nadler DL, 2014) Promotion occurs throughout the latent period and stimulates the growing cancerous cells to become a recognizable cancer. A third stage in the natural history of a cancer, referred to as Progression, involves maturation, differentiation or de-differentiation and accumulation of transcriptional changes that solidify the tumor's growth rate and invasiveness. Some carcinogenic substances are initiators and some are promoters, and still others are called complete carcinogens because they are capable of initiation and promotion.

c. Ovarian cancer

Ovarian cancer is a group of cancers that arise in the ovary or in adjacent tissues. It is estimated that about 22,240 women will receive a new diagnosis of ovarian cancer and about 14,070 women will die from ovarian cancer in the United States in 2018. (American Cancer Society, n.d.) (Torre LA, 2018) Ovarian cancer ranks fifth in cancer deaths among women, and first due to cancers of the female reproductive system. Most ovarian cancers are not discovered until they have reached an advanced stage and have spread to sites elsewhere in the body. Because advanced ovarian cancers are more difficult to treat, they have a high fatality rate. For these reasons, any effective prevention of ovarian cancer or reduction in ovarian cancer risk can have a significant impact on this disease and can save many women's lives.

There are several recognized forms of ovarian cancer that are distinguished by the specific tissues from which they arise, or the microscopic characteristics of the tumor cells themselves. About 85% to 90% of malignant ovarian cancers are epithelial ovarian carcinomas, and the majority of these are of the serous type (American Cancer Society, n.d.) (Prat, 2015). Ovarian, fallopian tube, and peritoneal cancers have a similar clinical presentation and are treated similarly, and current evidence suggests that they may have a common origin, supporting a common staging system (Soong TR, 2018).

Despite significant advances in cancer diagnosis and therapies over the past several decades, there have been few changes in the incidence or fatality rates for ovarian cancer. Consequently, it is worth considering preventable environmental causes of the ovarian cancer epidemic. (Woodruff, 1979) (LA Torre, 2018)

5. What is talc?

a. General

Talc is a hydrated magnesium silicate mineral produced through a metamorphic geological process and having the generalized chemical formula $\text{Mg}_3\text{Si}_4\text{O}_{10}(\text{OH})_2$. Some substitution of atoms occurs in variations of talc found in nature. Small amounts of Aluminum (Al) or Titanium (Ti) can substitute for Silicon, and small amounts of Iron (Fe), Manganese (Mn), Aluminum (Al) and Calcium (Ca) can substitute for Magnesium. This produces slight variations in the color, hardness and chemical properties of the mineral. Talc is the softest mineral on the Mohs Hardness Scale. (King, n.d.) It is essentially insoluble in water, but is slightly soluble in dilute mineral acids. The process seems to involve the extraction of magnesium and other cations leaving only the silicate as silicic acid and silica.

The commercial value of talc stems from its crystalline structure. Most talc is present in natural deposits as the platy form of talc, in which the talc crystals are arranged in large flat sheets running parallel to one another. These sheets are attracted to each other by weak Van der Waals forces that can be easily overcome by mechanical forces, causing the sheets to slide on each other. On the macro scale, this property gives talc its characteristic slippery feeling on the skin. The platy structure also gives talc its ability to absorb moisture and oil. Some talc is found as a fibrous crystalline structure, similar to some asbestos, also a magnesium silicate mineral. In fact, these two minerals are closely related in terms of their formation and composition. Talc deposits are often intermingled with asbestos and vice versa. (Rohl, 1974) (Rohl AN, 1976) (National Institute for Occupational Safety and Health, 2011) (Lockey, 1981)

b. Talcum Powder and Cancer.

Numerous studies have examined the cancer causing characteristics of talc. (Wild, 2006) Talc has caused cancer when implanted in various tissues and under the skin in laboratory animals. It causes inflammation and fibrotic reaction, including the chemotaxis of inflammatory immune cells, and accelerated growth and division of cells in the involved tissues (Okada, 2007). This is a normal body process that leads to the thwarting of infection and rapid healing, but in the absence of tissue injury, accelerated growth and cell division has the effect of amplifying and propagating viable genetic mutations, leading to cancer. Talc particles have been repeatedly demonstrated in ovarian tumor tissues (Henderson WJ C. J., 1971) (Henderson WJ T. H., 1979) and in inflammatory tissue in otherwise normal ovaries (Mostafa SAM, 1985). In 2006, the International Agency for Research on Cancer (IARC) evaluated the published evidence for the carcinogenicity of talc, not containing asbestiform fibers, when inhaled into the respiratory system and when applied to the perineum in personal hygiene activities. The agency concluded that talcum powder is a “possible human carcinogen” (Group 2B) when applied to the perineum, meaning that there is insufficient evidence of carcinogenesis in humans, but strong evidence in other mammalian species. IARC also concluded that there was insufficient evidence of carcinogenicity by the inhalation route (Group 3). (International Agency for Research on Cancer, 2010) Since that time,

numerous other studies have added to the data on this issue. A recent meta-analysis showed that talc workers do have an excess of lung cancers. (Chang C-J, 2017)

When implanted under the skin or into tissues of laboratory animals, talcum powder induces an inflammatory response. This reaction involves the chemotaxis of inflammatory cells of the immune system, lymphocytes, neutrophils and macrophages, the release of cytokines that promote membrane permeability and stimulate cell division. As this reaction matures over time, granulomas may begin to develop. All of this signifies that talcum powder is an effective and potent promotor of already initiated genetic alterations. (Fletcher NM M. I., 2018) (Fletcher NM S. G., 2018) (Saed GM, 2017) (Radić I, 1988) (Okada, 2007) Other studies have demonstrated the ability of these same reactions to satisfy the carcinogenic initiation step, characterizing talcum powder as a complete carcinogen. (Shukla A, 2009) (Fletcher NM M. I., 2018)

c. What about asbestos and other components in talc and talc-based products?

Talcum powder products in the marketplace have been shown to contain asbestos. (Paoletti L, 1984) (VanOrden D, 2000) (VanGosen BS, 2004) (Longo WE, 2017) Asbestos is conclusively recognized as a cause of ovarian cancers. The IARC Working Group concluded that “a causal association between exposure to asbestos and cancer of the ovary was clearly established, based on five strongly positive cohort mortality studies of women with heavy occupational exposure to asbestos, (International Agency for Research on Cancer, 2012)” and “studies showing that women and girls with environmental, but not occupational exposure to asbestos had positive, though non-significant, increases in both ovarian cancer incidence and mortality. (Acheson ED, 1982) (Fox, 1982) (Berry G, 2000) (Newhouse ML, 1972) (Reid A H. J., 2008) (Reid A S. A., 2009) (Pira E, 2005) (Magnani C, 2008) (Bertolotti M, 2008) (Ferrante D, 2007) (Germani D, 1999) (Rösler JA, 1994) The classification determined by IARC included all forms of asbestos and talc containing asbestiform fibers (fibrous talc). I have seen evidence that Johnson & Johnson’s talcum powder products contain asbestos and fibrous talc.¹

d. Carcinogenic metals in talcum powder

In addition to other related minerals, talcum powder may contain varying amounts of chromium, cobalt and nickel, metal ions that are recognized as cancer causing. These ions leach out of the talcum powder slowly over time, resulting in continuous, low-level exposure of the surrounding tissues to carcinogenic metals. (Jurinski JB, 2001) I have seen evidence that Johnson & Johnson’s talcum powder products contain nickel (Group 1

¹ Ex. 28, Hopkins Dep. (Aug. 16 & 17, 2018; Oct. 26, 2018; and Nov. 5, 2018); Ex. 47, Pier Dep. (Sept. 12 & 13, 2018); Expert Report of William E. Longo, PhD and Mark W. Rigler, PhD (Nov. 14, 2018)

human carcinogen), chromium (Group 1 human carcinogen), and cobalt (Group 2B-possible human carcinogen).²

e. Other potentially cancer-causing constituents

Johnson & Johnson's Baby Powder and Shower to Shower contain numerous ingredients that have been added to the products, i.e. fragrance chemicals, some of which have been shown to produce cancer in laboratory animals. These substances are likely to be present in very small or trace quantities, and likely present a lower level of risk than the major components, by mass. Nonetheless, any additional risks are added as part of a total risk profile. I have reviewed the report of Dr. Michael Crowley and agree with his conclusions that these chemicals may contribute to the inflammatory properties, toxicity, and potential carcinogenicity of the products.³

6. Epidemiology linking talcum powder and ovarian cancer

Many research studies have shown a strong association between talcum powder exposure and the development of ovarian cancer. (Langseth H, 2008) (Terry KL, 2013) (Schildkraut JM, 2016) (Trabert, 2016) (Berge W, 2017) (Cramer Daniel W, 2016) (Penninkilampi R, 2018)

a. What evidence links exposure to talcum powder products with ovarian cancer?

Multiple epidemiological studies have examined the link between the personal hygiene use of talc containing products and the occurrence of ovarian cancers (Booth M, 1989) (Cook LS K. M., 1997) (Cook LS e. a., 1997) (Cramer DW, 1982) (Whittemore AS, 1988) (Harlow BL W. B., 1989) (Chen Y, 1992) (Harlow BL C. D., 1992) (Rosenblatt KA, 1992) (Hartge P, 1988) (Tzonou A, 1993) (Chang S, 1997) (Heller DS, 1996) (Penninkilampi R, 2018). Talcum powder causes proliferation of human (Prat, 2015) ovarian cells in culture (Buz'Zard AR, 2007), and causes these cells to express reactive oxygen species (ROS) (Buz'Zard AR, 2007).

The research investigating the link between talcum powder exposure and ovarian cancer has been reviewed as a scientific whole at multiple stages. (Harlow BL H. P., 1995) (Ness Roberta B, 1999) (Muscat JE, 2008) (Terry KL, 2013) (Berge W, 2017) (Penninkilampi R, 2018)

Laboratory, animal and human studies support the conclusions that talc causes ovarian cancer, and have filled in the blanks that establish biological plausibility and scientific coherence. (Jaiswal M, 2000) (Balkwill Fran, 2001) (Okada, 2007) (Saed Ghassan M, 2017) (Harper, 2019)

7. Talcum powder product use

² Ex. 47, Pier Dep. (Sept. 12 & 13, 2018)

³ Expert Report of Michael Crowley, PhD (Nov. 12, 2018).

Numerous studies have interviewed women regarding their personal practices of application of talc-based powders to the perineal area. Due to variations in these practices, it has been difficult to estimate dose in order to evaluate the dose response relationship for ovarian cancer. It is also difficult to exactly estimate the quantity of talcum powder administration during personal hygiene activities. For studies that attempted to determine amount of exposure, most relied on a method of estimating the frequency of application and/or the duration of those practices, then simply multiplying to reach a total number of applications over time. (Harlow BL H. P., 1995) (Langseth H, 2008) A review of studies of perineal talcum powder or cornstarch application suggests that the use of cornstarch instead of talcum powder reduces the risk of ovarian cancer. (Whysner J, 2000)

8. Other evidence

- a. Transport of talc-containing materials from the perineum to the upper reproductive tract and body cavities has been shown to occur with startling regularity and with respect to a wide variety of particulate materials. (Egli GE, 1961) (Venter PF, 1979) (Blumenkrantz MJ, 1981) (Halme J, 1984) (Sjösten ACE, 2004) Clearly, sufficient particulate materials applied routinely to the perineum have ready access and in sufficient quantities to produce biological responses in internal tissues, including the ovaries and surrounding structures. There are a limited number of animal studies suggesting that this transport does not occur. (National Toxicology Program, 1993) These are not as compelling as the human evidence because of anatomical and physiological differences between animals and humans in this regard, as well as the overwhelming evidence in humans.

9. Conclusions and opinions

The following conclusions and opinions are expressed with respect to reasonable medical and scientific certainty and I have applied reliable scientific principles and methods to the facts in reaching them. These opinions are based upon the documents and literature reviewed and cited herein, and also upon my own professional training and experience in practice of medicine and medical toxicology.

I. Talcum powder products sold for personal hygiene use are carcinogenic.

Talcum powder is immunogenic, producing chronic inflammation in the tissues in which it sequesters, with the attraction of lymphocytes and macrophages and the ongoing local release of pro-inflammatory cytokines and reactive oxygen species. Further, all talcum powder has some component of mineral fibers that are toxic to macrophages and intensify the inflammatory response and stimulate cell growth and proliferation. The presence of asbestos, fibrous talc, carcinogenic metals and other chemicals further intensify this effect. Cohort and case-control studies have shown statistically significant associations between talc-based powder use and ovarian cancers. The presence of carcinogenic metals such as, chromium, cobalt and nickel, and toxic fragrance components in commercial talcum powder products, adds to their carcinogenic potency. Talcum powder is a complete carcinogen and can both initiate and promote the development of cancers in the tissues in which it sequesters.

II. Perineal use of talcum powder products for feminine hygiene purposes results in direct exposure to the female reproductive tract.

A proportion of talcum powder from personal hygiene applications to the perineum is transported or migrates through the reproductive tract, through the patent fallopian tubes, onto the ovaries and into the pelvic cavity. Talc particles have been identified in reproductive system structures of women who utilize talc powders. These include the uterine cervix, the endometrium, the fallopian tubes and the ovaries. Inhalation is likely a secondary route of exposure.

III. Common carcinogenic constituents of talcum powder products participate in and add to the carcinogenic process.

Naturally occurring carcinogenic components of talcum powder, i.e. asbestos, chromium, nickel, and cobalt, are liberated in bodily fluids and tissues and are free to exert their carcinogenic effects. Added substances that are toxic or carcinogenic, i.e. fragrance chemicals, may also contribute to these effects. This process is the most intense where the duration is the longest. Because the ovaries have no intrinsic elimination system, the transport of talc particles and their constituents reaches the ovaries where it stalls and sequesters. For these reasons, ovarian tissue is most at risk for the carcinogenic effect of these substances.

IV. Regular perineal application of talcum powder products causes epithelial ovarian cancer in some users, and raises the risk of ovarian cancer in all users.

Multiple case-control and cohort epidemiological studies have looked at the relationship between the perineal use of talc-based powders and the eventual development of epithelial ovarian cancer. Most, but not all, of these studies show a consistent positive relationship. When confounding and bias are exhaustively considered, the positive association remains. I conclude that the apparent cause and effect relationship between perineal talcum powder use and ovarian cancer is real, amounting to about a 30% increased risk of ovarian cancer in talcum powder product users. At the current rate of ovarian cancer diagnosis and mortality, elimination of this source of risk could result in over 3,000 lives saved in the U.S. each year.

In 1965, Sir Austin Bradford Hill published what has come to be recognized as the best collection of factors to consider for the assessment of scientific evidence that relates the causation of disease to environmental exposures (Hill, 1965). These factors include: (1) Strength of association, (2) Consistency of the evidence, (3) Specificity, (4) Temporality, (5) Biological gradient, (6) Plausibility, (7) Coherence, (8) Experiment, and (9) Analogy. Below I provide my evaluation of the scientific evidence with respect to the Hill factors.

Strength of association –Many epidemiological studies have attempted to examine the association between perineal use of talcum powder products and ovarian cancer. Most of these have been case-control studies, where women diagnosed with ovarian cancer are paired with others of similar demographic background who do not have ovarian cancer. All of these women are interviewed about their past practices and exposures, including the use of talcum powder products. The resulting data are analyzed to compute an odds ratio (OR) that describes the

likelihood of those with cancer having had greater exposure to talcum powder than those who did not. Cohort studies selected populations of women, assessing them for many factors, including perineal talcum powder use, and followed them over time counting the occurrences of ovarian cancers. These studies were then able to compute a relative risk (RR) of exposure to talcum powder resulting in ovarian cancers. Of more than 25 case-control studies in the literature, the heavy majority showed positive and significant ORs for perineal talcum powder use and ovarian cancer. The three cohort studies did not find a significant relative risk of perineal talcum powder exposure leading to ovarian cancer, but did show positive non-significant trends. Several research groups have looked at the totality of the research evidence, evaluated the published study reports, and have reanalyzed those data on a common playing field through meta-analyses. Taken in their totality, and accounting for sources of bias and differing statistical treatments, these epidemiological studies support a strong association between the perineal use of talcum powder and ovarian cancer.

Consistency of the evidence – As stated above, the majority of epidemiological studies that have investigated the link between perineal talcum powder use and ovarian cancer have reported positive associations. These studies are consistent in their findings of a relationship between perineal use of talcum powder products and the development of ovarian cancer. Further, recent meta-analyses of previously published studies have verified the comparability of the research methods used and the consensus of conclusions.

Specificity – Specificity is the concept that a specific disease, rather than a host of diseases, is produced by a particular exposure, and that the exposure is a principal cause of the disease. Although talcum powder is known to cause non-specific inflammation in many tissues where its residues locate, the stimulation of ovarian cancer is particularly associated with the presence of talc in the ovaries and fallopian tubes. Of known factors associated with ovarian cancer, i.e. nulliparous state, early menarche, late menopause, oral contraceptive use, living in the twentieth century and beyond, perineal talcum powder exposure is proving to be prominent among them.

Temporality – If a particular exposure is the cause of a particular disease, then the onset of exposure should precede the onset of the disease. Studies investigating the link between perineal talcum powder exposure and ovarian cancer are designed to compare those with prior exposure to those who are not exposed, and so the scientific evidence supports this consideration.

Biological gradient – A basic toxicological principle is that a greater exposure intensity will result in a larger proportion of those exposed expressing the toxic effect, in this case ovarian cancer. In order to determine the intensity of a long-term environmental exposure, typically a measure of frequency or quantity of use is multiplied by the duration of such use. This allows categorization of exposure levels and comparisons. Although some studies have failed to find evidence of a dose-response relationship, several more recent reports have shown a clear dose-response when the number of subjects rose to a level producing sufficient statistical power to allow the analysis after subdivision of subjects into pertinent categorical groups, and frequency and duration were measured (Schildkraut JM, 2016) (Cramer Daniel W, 2016) (Wu, et al., 2009).

Plausibility – This factor expects the rational presentation of a mechanism whereby the exposure in question leads to the disease. Thus, if no such mechanism can be proposed, it is less likely that causation will be supported. In the case of ovarian cancer, the mechanism supported in the literature is as follows: Talcum powder products are applied to the perineal area in the course of routine personal hygiene practices. This element is supported by the existence of these products in the marketplace for many years and the statements of subjects interviewed for the purpose of conducting the scientific research discussed elsewhere in this report. Portions of the applied powders are transferred via active processes or passive mass action movements into the female reproductive tract, some making it all the way to the distal fallopian tubes, the ovary surfaces and the pelvic and peritoneal cavities. This element is supported by the observations that particulate materials of differing variety can make their ways along these pathways to the listed destinations, and the finding and confirmation of talc particles in normal ovarian tissues and ovarian tumor tissues at the time of oophorectomy or autopsy. Once reaching the target tissues, talcum powder and its constituents initiate carcinogenesis via multiple means, including, inflammation with chemotaxis of inflammatory cells, liberation of cytokines, and reactive oxygen species, inactivation of TP53 genetic modulator, inhibition of DNA repair, and long-term promotion of genetic mutations via continuous inflammation and cellular growth stimulation.

Coherence – The proposed cause and effect relationship should not “seriously conflict with the generally known facts of the natural history and biology of the disease.”(Hill, 1965) The proposal that talcum powder product use results in the occurrence of ovarian cancer is entirely consistent with what is known about other factors related to ovarian cancer, i.e. early menarche, late menopause, pregnancies, breastfeeding history, oral contraceptive use, etc. All are factors that influence the local inflammatory environment of the ovary and its surroundings and have the potential to promote existing transcriptional errors and mutations.

Experiment – Interventions, such as tubal ligation that decreases the incidence of ovarian cancer by blocking the exposure route, offers experimental support for this mechanism. The use of cornstarch-based dusting powders as a substitute for talcum powder products offers additional experimental support.

Analogy – Have there been other environmental exposures that have been associated with ovarian cancers that act via similar mechanisms? Talcum powder is somewhat unique in terms of its delivery mechanism. But beyond that, the case of asbestos exposure is similar. Asbestos exposure has resulted in excesses of ovarian cancers in exposed women, although the route of exposure is thought to be by inhalation. Nonetheless, asbestos is a mineral very similar both chemically and structurally to talc that has been found in the ovary and peritoneal cavity of exposed women. The mechanisms of carcinogenesis for both asbestos and talc are similar and analogous. Further, talc-based products contain asbestos and non-asbestos mineral fibers having carcinogenic potential.

When considering these factors, I gave the most weight to the compelling strength of association and consistency, as well as the well-described biologic mechanism.

The currently available scientific research, when considered in its totality, demonstrates a cause and effect relationship between the use of talcum powder products and the development of epithelial ovarian cancer. This opinion is reinforced by my consideration of the Hill factors for the assessment of causation.

In reviewing the scientific and medical literature on talcum powder product use, I also performed a risk assessment and considered whether perineal use of those products poses a safety risk to consumers. This involved careful consideration of the epidemiological literature, data on the dose-response relationship and exposure, as well as the nature of these products, which are used primarily for personal care. I also considered evidence of the toxicity of these products, for which repeated testing and analyses have shown to contain carcinogens.

In considering the weight of this epidemiologic, toxicologic, and mechanistic evidence, across multiple studies, time, demographics, and researchers, demonstrating a consistent association between perineal use of talcum powder products and ovarian cancer, it is my opinion that talcum powder products increase the risk of ovarian cancer and pose a significant health hazard.

In conclusion, it is my opinion that the perineal use of talcum powder products causes ovarian cancer in some users and increases the risk of ovarian cancer in all users of these products.

All of my opinions in this report are provided with respect to a reasonable degree of medical and scientific certainty. I reserve the right to amend or supplement my report as new information becomes available.

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Exhibit A

Curriculum Vitae

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Biosketch

Arch "Chip" Carson, MD, PhD is a physician (The Ohio State University), board certified in Occupational Medicine (American Board of Preventive Medicine), who holds a Doctor of Philosophy degree in Toxicology (University of Cincinnati, Kettering Laboratory). He has served on the faculty of the University of Cincinnati and the New York University Medical Center and joined the faculty of the University of Texas School of Public Health in 1992 in its Environmental Sciences Discipline and Occupational and Environmental Health and Aerospace Medicine Module. He is Associate Professor of Occupational Health, directs the Occupational and Environmental Medicine Residency Program and is a member of the research team of the Southwest Center for Occupational and Environmental Health, a NIOSH Education and Research Center, and WHO Collaborating Centre in Occupational Health. He maintains a clinical practice of occupational medicine and medical toxicology. In his more recent role as Medical Director for the University of Texas Medical Branch in Galveston, he is responsible for the health monitoring and care of more than 15,000 employees. He is a frequent consultant to governments, corporations and the legal community on matters related to industrial chemical exposure, toxicology and environmental justice. His research interests include: environmental and occupational chemical exposures, inhalation injuries, metal exposures and cancer, and professional training in occupational medicine.

Professional Activities/Employment

2017-18	University of Texas Medical Branch, Galveston, Assistant Clinical Professor of Preventive Medicine and Family Medicine
2017-18	University of Texas Medical Branch, Galveston, Medical Director, Employee Health Services.
2017-18	Enbridge Corporation, Houston Texas, Medical Director, Employee Health Services.
2010-18	University of Texas Health Science Center, Houston, Associate Professor of Occupational Health.
2010-18	University of Texas Health Science Center at Houston, Program Director, Occupational and Environmental Medicine Residency.
1991-18	Private practice of Occupational Medicine and Toxicology, New York, Texas and Ohio.
2011-18	Spectra Energy Corporation, Houston Texas, Medical Director, Employee Health Services.
1997-13	Texas Medical Center Inc., Houston Texas, Medical Director, Employee Health Services.
1992-08	University of Texas School of Public Health, Assistant Professor of Occupational Medicine and Environmental Sciences.
1998-08	University of Texas Health Science Center at Houston, Program Director, Occupational and Environmental Medicine Residency.
2003-08	Southwest Center for Occupational and Environmental Health, Principal Investigator and Director, Diller Phosgene Exposure Incident Registry of the American Chemistry Council.

2000-06	Chevron Phillips Chemical Company, Houston Texas, Corporate Medical Director.
2003-05	U.S. Department of Energy Office of Worker Advocacy Physician Review Panel Appointee.
1997-04	Southwest Center for Occupational and Environmental Health, Principal Investigator, City of Houston Lead Poisoning Epidemiology Project.
1992-03	UT Health Services, University of Texas Houston Health Science Center, Attending Physician, Occupational Medicine and Toxicology.
1997-01	University of Houston Downtown, Medical Director, Student Health Service.
1998-99	University of Texas School of Public Health, Convener of the Occupational/Environmental Health and Aerospace Medicine Module.
1992-97	Respiratory Consultants of Houston, PA, Attending Physician, Occupational Medicine and Toxicology.
1992-95	Exxon Chemical Americas, Baytown Polymer Center and Basic Chemicals Technology, Baytown TX, Consultant Physician.
1990-91	New York University Medical Center, Bellevue Hospital, Tisch Hospital, and Manhattan VA Hospital, New York NY, Dept. of Medicine, Clinical Instructor.
1982-90	Chemical Information Services Inc, Cincinnati OH, Associate in Toxicology.
1978-87	University of Cincinnati College of Medicine, Cincinnati OH, Instructor and Lecturer, Adjunct Assistant Professor of Industrial Toxicology.
1974-79	University of Cincinnati College of Medicine, Kettering Laboratory, Cincinnati OH, Research Technologist in Occupational Medicine and Clinical Studies.
1969-74	Millstone Inc., Cincinnati OH, Design Engineer, environmental control systems.

Educational Background

2002	Certificate of Board Eligibility, Medical Toxicology, American Board of Preventive Medicine/American Board of Emergency Medicine
1992	Certificate of Training - Residency in Occupational Medicine University of Texas Health Science Center at Houston, School of Public Health, and Southwest Center for Occupational and Environmental Health, Houston TX, 1992.
1991	Certificate of Training - Postgraduate Internship in Internal Medicine, New York University Medical Center and Bellevue Hospital Center, New York NY.
1990	MD - Ohio State University College of Medicine, Columbus OH.
1987	PhD - Kettering Laboratory, University of Cincinnati College of Medicine, Cincinnati OH, awarded in the field of "Environmental Health – Toxicology."
1973	BS - University of Cincinnati College of Arts and Sciences Cincinnati OH. Awarded in "Biological Sciences with Concentration in Engineering."
1969	Rensselaer Polytechnic Institute, Troy NY. Management Engineering
1968	Villa Madonna College, Covington KY. Certificate in Contemporary Physics.

Fellowships

2011-13	UTHealth, Health Educators Fellowship, University of Texas Health Science Center at Houston.
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- 1983-85 American Lung Association Fellowship in Lung Research (Inhalation Toxicology), American Lung Association of Southwestern Ohio, Grant.
- 1981-82 Owens Corning Fiberglas, Graduate Research Fellowship in Combustion Toxicology.
- 1979-80 National Institute for Occupational Safety and Health, Centers for Disease Control, Doctoral Fellowship in Industrial Toxicology.

Certifications

- 2012 License to practice medicine, State of Ohio 35.098635
- 2010 Certified Healthy Homes Specialist – National Environmental Health Association.
- 2002 Board Eligibility, Medical Toxicology, American Board of Preventive Medicine/American Board of Emergency Medicine.
- 1994 Board Certification, Occupational Medicine, American Board of Preventive Medicine.
- 1992 License to practice medicine, State of Texas J2524.
- 1991 License to practice medicine, State of New York 186563.
- 1982 Emergency Hazard Response, Environmental and Industrial Chemical Accident Management, U.S. Environmental Protection Agency.
- 1979 Pulmonary Function Testing for Occupational Surveillance, NIOSH #003.

Professional Community Service

- 2013-18 University of Texas Health Science Center at Houston, Steering Committee on Interprofessional Collaboration
- 2013-18 University of Texas Health Science Center at Houston, Chemical Safety Committee.
- 1998-18 Association of Environmental and Occupational Clinics/ATSDR community resource on toxic exposures and health consequences, Federal Region VI.
- 1997-18 City of Houston Biological, Chemical and Radiation Emergency Preparedness Program. Medical Toxicology On-Call Advisor to the Houston Medical Strike Team.
- 1998-18 Association of Occupational and Environmental Medicine Residency Directors. Chairman 2005-2006
- 2010-18 University of Texas Health Science Center at Houston, Graduate Medical
1997-08 Education Committee
- 2010-18 University of Texas Health Science Center, Houston, Community/Press
1994-08 Resource and Speaker via Public Information Office, (Toxic Exposures and Environmental Health).
- 1996-18 American College of Occupational and Environmental Medicine, Council on Academic Affairs and Co-chair, Academic Section 2004-2006. Occupational Medicine Residency Directors Committee, Chair 2006-2007, Appointed Member, Taskforce on the Future of Occupational Medicine Education 2005-2007. Appointed Co-chair, Taskforce on the Future of Occupational Medicine Education 2013-2015.
- 1996-18 Texas College of Occupational and Environmental Medicine. Secretary/Treasurer-2004-5, President Elect-2005-6, President-2006-7, Past President 2007-8.
- 2003-12 Boy Scouts of America, Sam Houston Council, Registered Adult Leader and Merit Badge Counselor.
- 2005-08 University of Texas School of Public Health, Practice Council Co-chair

2003-05	U.S. Department of Energy Office of Worker Advocacy Physician Review Panel Appointee.
1996-00	American Public Health Association, Occupational Health Subcommittee
1994-96	Advisory Board, National Environmental Education and Training Center (NEETC), Curriculum Development Committee.
1981-85	Tri-State Air Committee Inc., Cincinnati OH, (voluntary air quality organization) Scientific Advisor, Elected to Board of Directors in 1982, President and Chairman 1984-85.
1981-85	American Lung Association of Southwestern Ohio, Cincinnati OH, (voluntary health organization) speakers bureau.
1982-83	City of Cincinnati, Appointment to Occupational Health Scientific Liaison Board (municipal advisory committee).
1981-83	Cincinnati Area Toxic Substances Coalition, Cincinnati OH, (coalition of business, voluntary, and labor organizations with interest in environmental toxic substance issues) Cofounder and Chairman.
1982-83	Ohio River Valley Committee on Occupational Safety and Health, Cincinnati OH, (organized labor coalition) Scientific Resource Committee.
1972-82	Walnut Hills-Evanston Medical Center, Cincinnati OH, (primary care center) Board of Directors.

Professional Societies

1991-18	American College of Occupational and Environmental Medicine.
1991-18	Texas College of Occupational and Environmental Medicine
2007-18	Texas Public Health Association.
2006-18	International Congress on Occupational Health.
2003-18	American College of Medical Toxicology.
2002-06	Society of Occupational and Environmental Health.
2001-06	American Conference of Governmental Industrial Hygienists.
1994-00	American Public Health Association.
1983-87	American Industrial Hygiene Association.
1983-87	Society of Toxicology.
1980-85	American Thoracic Society, Associate Member and Participant in Occupational and Environment Scientific Session.

Publications

Anderson F, **Carson A**, Whitehead L and Burau K Age, Race and Gender Spatiotemporal Disparities of COPD Emergency Room Visits in Houston, Texas. Occupational Diseases and Environmental Medicine. 3:1-9, 2015. <http://dx.doi.org/10.4236/odem.2015.31001>.

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Calcote, JC, **Carson, A**, Peskin, MF, Emery, RJ. An assessment of post-disaster psychological stress in hazardous waste operations and emergency response (HAZWOPER) workers. *Disaster Med Public Health Preparedness*. 7:452-460, 2013. PMID 24274124.

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Nooka A, Duonghi L, **Carson A**, Hassan M. Assessing Occupational Risk for Pancreatic Cancer by Chemical Exposures and Work History: A Case-Control study at MD Anderson Cancer Center. American Association for Cancer Research, Orlando. March, 2004.

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Carson A, Guevara E, Delclos GL, Murray KA, Burau KD, Morandi MT, Felknor SA, ("A Study of General Health of Workers of the Industrial Complex of Barrancabermeja") in [Compendium on Occupational Health in the Petroleum Industry of Colombia: Technical and Scientific Report of the "Occupational Health in the Petroleum Industry" Project], 1999 Pan American Health Organization (co-author).

Carson A, Hangoc V and Bahrainwala M, City of Houston Childhood Lead Poisoning Prevention Program: Case Density and Impact Analysis, June 30, 1999, Technical Report (Principal Investigator).

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DEPOSITIONS, TRANSCRIPTS AND REPORTS:

Affidavit of Laura Plunkett, PhD 02.22.18

Deposition of Alice Blount in the Ingham v. J&J Matter on 04.13.18

Deposition of Annie Awanaiss Yessian on 07.13.2017

Deposition and Exhibits of Pat Downey Dated 8.7.18-8.8.18
Deposition and Exhibits of John Hopkins Dated 8.16.18-8.17.18, 10.17.18 and 11.05.18
Deposition and Exhibits of Susan Nicholson Dated 7.26.18-7.27.18
Deposition and Exhibits of Julie Pier Dated 9.12.18-9.13.18
Ingham v. J&J Volume 11 (Egilman, Koman, Martinez, Packard) 6-14-18
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Laura Plunkett - Supplemental Expert Brower Report
Longo Analysis of J&J's Historical Talc Samples from the 1960's
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Exhibit 1 - ATTORNEYS' EYES ONLY
Exhibit 2 - ATTORNEYS' EYES ONLY
Exhibit 3 - ATTORNEYS' EYES ONLY
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Fitzgerald Analysis of J&J Baby Powder #1 and #2 Dated July 26, 2017
IARC Monograph 100C - Arsenic, Metals, Fibres, and Dusts - Excerpts
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IMERYS210729	JNJ000064544
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IMERYS286445	JNJ000065264
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IMERYS340798	JNJ000087716
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IMERYS422289	JNJ000237076
IMERYS 088907	JNJ000237379
IMERYS 284935	JNJ000239723
IMERYS137677-IMERYS137690	JNJ000239730
IMERYS209971	JNJ000245002
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JNJ000251888

JNJ000260700

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JNJ000265536

JNJ000279507

JNJ000348778

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No. 421

P-468

Read-the-Letter-from-the-FDA-on-Cosmetics

The Birth of Our Baby Products _ Kilmer House

WCD 002478 - Exhibit 32 Waldstreicher

JNJ000460665

JNJ000526750

JNJ000886067

JNJAZ55_000000577

JNJAZ55_000000905

JNJAZ55_000004563

JNJAZ55_000008177

JNJL61_000014431

JNJMX68_000003728

JNJMX68_000012858

JNJMX68_000013019

JNJNL61_000079334

Arch Carson, MD, PhD Legal Testimony, 2015-2018

Elaine Hale and Kenneth Dorsey parker, Jr. v. Centerpoint Energy Houston Electric, LLC; in the 55th
District Court of Harris County, Texas.

2016 Harris County, TX for Plaintiff

Danny Henderson and Linda Henderson; Magdaleno Flores and Maria Flores; Shari Waldrop; and Bryan
Thomas v. Magnablend, Inc., Nugreen Specialty, Inc., Nugreen Solutions, Inc., and Enviro Tech Inc.; in
the 40th District Court of Ellis County, Texas.

2015 Ellis County, TX for Defendant

Edgar Guadalupe Solis v. Eastman Chemical Company, Texas Operations, Tradebe Environmental
Services, Inc. d/b/a Tradebe Industrial Services LLC; in the 234th District Court of Harris County, Texas.

2015 Harris County, TX for Defendant

Arch I. Carson, MD, PhD
Professional Consultation Fee Schedule

Evidence-base research, report preparation, documentation, conference	\$450/hr
Interview, physical examination or medical testing of patients	450/hr
Review of documents	450/hr
Testimony at deposition or trial plus expenses	450/hr
Inspection, examination or sampling of physical evidence or sites	450/hr
Travel (Travel maximum \$4,000 per diem, plus expenses)	200/hr
Laboratory analyses/studies	at cost
Overhead and Supplies	at cost

Exhibit 7

**UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY**

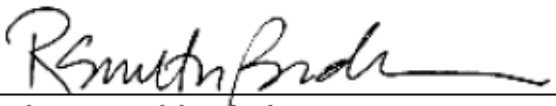
**IN RE JOHNSON & JOHNSON
TALCUM POWDER PRODUCTS
MARKETING, SALES PRACTICES,
AND PRODUCTS LIABILITY
LITIGATION**

MDL NO. 16-2738 (FLW) (LHG)

THIS DOCUMENT RELATES TO ALL CASES

**RULE 26 EXPERT REPORT OF
REBECCA SMITH-BINDMAN, MD**

Date: November 15, 2018



Rebecca Smith-Bindman, MD

The Relationship Between Exposure to Perineal Talc Powder Products and Ovarian Cancer

Expert Report

Rebecca Smith-Bindman, MD

Professor, Radiology and Biomedical Imaging, Epidemiology and Biostatistics, Obstetrics,
Gynecology and Reproductive Science and Director, Radiology Outcomes Research Lab
University of California San Francisco

Table of Contents

<i>I. Executive Summary.....</i>	<i>4</i>
<i>II. Expertise of Dr. Smith-Bindman.....</i>	<i>6</i>
Education and Employment	6
Research Expertise.....	6
Knowledge of Relevant Study Designs	6
Experience as a Medical Expert.....	8
<i>III. Background: Ovarian cancer and Talc as a Modifiable Risk Factor.....</i>	<i>8</i>
Ovarian Cancer	8
Histologic types	9
Risk Factors	11
Etiology: Origins, Causes, Development and Inflammation	12
Association of Ovarian Cancer with Talc Powder Products	13
Why Talc Powder Products were Initially Suspected as Causing Ovarian Cancer.....	13
Asbestos	14
Talc.....	15
Heavy Metals.....	16
<i>IV. Overview of Publications on Genital use of Talc powder products and Ovarian Cancer.....</i>	<i>16</i>
Explanation of study designs and article types	16
Table of Reviewed Publications	18
Quantifying Exposures	19
Summary of Data	19
Cohort Studies	19
Systematic Reviews	22
Pooled Data	27
Case-Control Trials.....	29
<i>V. Rationale for and Explanation of the New Systematic Review.....</i>	<i>30</i>
<i>VI. New Systematic Review of Literature Quantifying Association Between Regular Frequent Genital (Perineal) Talc powder products Application and Ovarian Epithelial Cancer Risk with A Focus On Invasive Serous Cancer.....</i>	<i>31</i>
Literature Search	31
Article Selection.....	31
Exclusion	32
Defining Talc powder products Use.....	32

Stratification of Analyses: Focus on a Single Histologic Type Where Possible	32
Type of Exposures.....	32
Statistical Analysis	33
Results.....	33
New Systematic Meta analytic review: Summary.....	34
Overall Summary of the Epidemiology Data Describing the Association Between Talc Powder Products and Ovarian cancer	34
<i>VII. Other Relevant Factors</i>	<i>35</i>
Research Supporting Talc Association with Ovarian Cancer: Transit to ovary and Risk Reduction on Interruption.....	35
Interactions	32
Risks Over Time	32
Variation in Risk when Talc Use is Discontinued.....	35
<i>VIII. Consideration of Causality of Talc powder products and Ovarian Cancer : Bradford Hill Factors</i>	<i>35</i>
A) Strength of Association.....	36
B) Consistency of Associations in Different Populations and Studies	38
C) Specificity Between Cause and Outcome	39
D) Temporality.....	39
E) Dose Response.....	39
F) Biologic Plausibility: Factors Linking Talc and Ovarian Cancer	40
G) Coherence and Consistency with Understood Biology.....	41
H) Experimental Evidence	41
I) Analogy	41
<i>References</i>	<i>42</i>

I. Executive Summary

Substantial evidence supports a strong positive association between ovarian cancer and genital exposure to talcum powder products and that regular exposure to talcum powder products causes ovarian cancer in some women. Talc is a naturally occurring mineral used in cosmetic products because of its desirable chemical properties such as being soft and absorbent. Women who have had regular exposure of the genitals (specifically the perineal region from the pubic area to the anal area) to talcum powder products are at increased risk of developing invasive ovarian cancer, in particular serous cancer, the most common and most lethal form. In the United States, a substantial portion of women report having ever used talc powder products at some point in their life. The most commonly reported frequency of talcum powder product use is daily. Women who use talcum powder products daily increase their risk of developing ovarian cancer significantly. Regular exposure causes ovarian cancer in some women.

I was asked to review the medical and scientific literature regarding the relationship between genital talcum powder product use and ovarian cancer and determine whether the relationship is causal. For this extensive analysis and report, I applied the same methodology with the same scientific rigor that I use in my research and clinical practice. I reviewed 43 relevant publications presenting scientific data on the association between ovarian cancer and exposure to talc powder products: 4 cohort studies, 8 systematic reviews, 2 studies that pooled data from multiple individual studies, and 30 case-control studies. I also read numerous review articles, and systematic reviews on related topics such as those completed by the International Agency on Research on Cancer (IARC). I also completed my own, new systematic review on of the studies that I reviewed as part of this report. This report contains my overview of these publications plus a detailed new systematic review of the studies that I conducted. After reading, evaluating, and summarizing these publications, in my expert opinion, I do not have any uncertainty that regular exposure to talc powder products increases a woman's chance of developing epithelial ovarian cancer. In my expert opinion, regular exposure to talcum powder products causes ovarian cancer

Quantifying the precise magnitude of the association is more difficult than establishing the association. The association will certainly vary by demographic and reproductive factors and whether women have other underlying ovarian cancer risk factors and exposures. With that caveat, **it is my opinion that women exposed to perineal talc powder products on a regular basis have about a 50% increase in their subsequent risk of developing invasive serous ovarian cancer**, compared to women who do not regularly use talc and even after accounting for other ovarian cancer risk factors. This estimate is supported by existing publications and my quantitative review of the scientific literature that focused on summarizing studies that addressed regular exposure to talc powder products as a risk factor for epithelial ovarian cancer, and in particular serous cancer. Talcum powder exposure is associated with other epithelial cancer subtypes (in particular, clear cell and endometrioid carcinoma), but because these cancers are less common, and because fewer studies have evaluated these cancers in sufficient numbers, quantifying the associations is more difficult. While some publications estimated talc powder products have a slightly greater risk of these cancer subtypes, others

estimated a slightly lower risk of these cancer subtypes. In my opinion, this risk is likely overall in about the same range as for serous cancer, but I would estimate slightly less at 40% increased risk.

The epidemiological evidence documents a strong, positive association between exposure to talcum powder products and ovarian cancer and that regular exposure causes ovarian cancer. The epidemiological evidence alone does not confirm the mechanism by which talc powder product increases ovarian cancer risk, nor does it confirm the specific component in talcum powder products that makes it carcinogenic. Nonetheless, the literature provides compelling evidence that exposure to talcum powder products leads to chronic inflammation and that the inflammation induces a strong biological response that results in the induction, promotion, and growth of cancer. Further, there is evidence that several highly carcinogenic agents are components of the talcum powder products. These include, most importantly, asbestos, a Group 1 carcinogen that the International Agency for Research on Cancer (IARC) has determined causes ovarian cancer. I have seen evidence that talcum powder products contain asbestos. Second, talcum powder products contain asbestiform talc particles which have a similarity in structure to asbestos fibers (and which IARC concludes are carcinogenic). Lastly, talcum powder products contain numerous heavy metals such as, nickel, chromium, (Group 1 carcinogens) and cobalt (Group 2 carcinogen) according to IARC. These components are carcinogenic (cause cancer) and can contribute to the carcinogenicity of talcum powder products. Observational and experimental data confirm that talcum powder product particles applied to the perineum can reach the fallopian tubes and ovaries through the vagina, supporting that talc particles applied to the perineum can deposit on the ovaries. Surgery that impedes the movement of particles from the perineum to the ovaries such as hysterectomy (uterine removal) or tubal ligation (tying or blocking the fallopian tubes to the ovaries), reduces the elevated risk of ovarian cancer from exposure to talcum powder products. This finding supports that local tissue response and inflammation in the fallopian tubes and/or ovaries from talcum powder products (with components) causes the elevated ovarian cancer risk.

In summary, **from my review of the scientific literature and my own analysis, it is my opinion that genital exposure to talcum powder products is an actionable and causative risk factor for ovarian cancer.** As a physician involved in women's health issues, I view talcum powder usage as a modifiable "lifestyle" risk factor that should be avoided because of the substantial risk to health and lack of therapeutic benefit. An elevated risk of 50% is significant and results in a large number of unnecessary ovarian cancers given the large number of women exposed. Depending on estimates of how many women regularly use talcum powder products, between 7% and 20% of all ovarian cancers and 14% - 39% of invasive serous cancers (the most aggressive and feared cancer type) are caused by the use of talcum powder products. These cancers can be prevented if women do not use talcum powder products.

II. Qualifications

Education and Employment

I am a professor of Radiology and Biomedical Imaging, Epidemiology and Biostatistics, Obstetrics, Gynecology and Reproductive Medicine, and Health Policy at the University of California San Francisco (UCSF) School of Medicine. I graduated from Princeton University with a degree in structural engineering (with combined majors in engineering and architecture) and attended UCSF medical school. My training after medical school included an internship, radiology residency, and clinical fellowship in women's health and a research fellowship in epidemiology and biostatistics in the UCSF Departments of Medicine and Epidemiology and Biostatistics.

I am a clinician-scientist. My clinical work includes one day a week in the Department of Radiology and Biomedical Imaging, with a focus on women's health imaging. I work in the ultrasound section, where a large proportion of the work is focused on the diagnosis of ovarian abnormalities (cancer and other functional issues). I run the UCSF Radiology Outcomes Research Lab, spending most of my time on clinical research and leading large epidemiological studies. I teach in the UCSF School of Medicine and Department of Epidemiology and Biostatistics.

Research Expertise

My research expertise is in epidemiology, outcomes research, comparative effectiveness, health services research, and dissemination and implementation sciences. My epidemiological studies have evaluated the quality, use, accuracy, predictive value, and impact of diagnostic testing on patient health. I have measured the risks and benefits of medical imaging in different contexts and different populations. Much of the research is in women's health, including diagnoses of cancers such as ovarian, endometrial, thyroid and breast. I have led many large, multi-institutional research projects. These projects are typically collaborative, involving researchers and clinicians with diverse expertise including radiology, obstetrics and gynecology, medicine, biostatistics, epidemiology, economics, demography, social sciences, medical informatics, radiation science, and dissemination and implementation science.

I have been a prolific researcher. I have led projects funded by more than 50 million dollars in research grants—entirely focused on cancer diagnosis and prediction. The research has been published in the most prestigious medical journals including the *New England Journal of Medicine*, *Annals of Internal Medicine*, *Journal of the American Medical Association*, *Journal of the American Medical Association Internal Medicine*, *Journal of the National Cancer Institute*, *Obstetrics and Gynecology*, and leading radiology specialty journals such as *Radiology* and *Journal of the American College of Radiology*.

Knowledge of Relevant Study Designs

Several of my published studies have been systematic, meta-analytic, quantitative reviews of the published literature. Meta-analyses review existing evidence on a topic and summarize

and re-analyze data from earlier studies. My systematic reviews focused on the diagnoses of endometrial cancer, breast cancer, and a range of birth defects including trisomy 21 (Down syndrome) and trisomy 18 (Edwards Syndrome). Many of my reviews were published in prestigious medical journals, reflecting their scientific rigor based on an in-depth understanding of how to combine and review results from different studies in a scientifically valid and reproducible way.

Several of my recent research projects quantified the variation in radiation dose associated with medical imaging and the expected impact of this variation on cancer outcomes. This work has brought attention to the need for better standards in medical imaging. I am currently leading two large, multi-institutional epidemiological projects on medical radiation funded by the National Institutes of Health. One project is collecting radiation dose measures associated with computed tomography (CT) imaging from more than 150 hospitals in the United States, Europe, and Asia and testing the impact of providing feedback and education to radiologists on average and high doses. The second project is a multinational epidemiological study on childhood cancer. This project is assessing the risk of cancer associated with medical imaging among 1 million children and 1 million pregnant patients after accounting for a range of other cancer risk factors. The study will be the first to quantify the risk of medical imaging including CT among a large group of patients and uses novel methods to accurately estimate radiation dose from imaging.

I have expertise in a range of research study designs. The projects I currently lead (each funded by the National Institutes of Health or the Patient-Centered Outcomes Research Institute for between 9 - 15 million dollars each) have designs selected to be appropriate for the research question. For example, the study assessing the risk of cancer from medical imaging uses a *case-control study design, in which data are collected on a group of patients and those with a condition (cases), are matched to similar patients without the condition (controls)*. Matching people with a disease to people of similar age, gender, and other factors who do not have the disease allows researchers to determine if circumstances such as exposure to a potential toxin influence disease development.

My project on medical imaging uses a *cohort design, comparing groups of people (cohorts) in a population, some exposed to a potential disease agent and some not exposed*, to see if the agent influences disease. My study on radiation doses from CT uses a *randomized controlled design, in which individual patients are randomly assigned to different treatments* so their effectiveness can be compared. I am studying lung nodules using a *cluster-randomized controlled trial design that randomly assigns groups of people in similar circumstances (for example because they all see the same doctor) to different treatments* so the effects of the treatments can be compared.

I have a deep understanding of how epidemiological studies are conducted. I understand what study designs are suitable to particular datasets, populations, and research questions and the advantages and disadvantages of each design. This is relevant as no single study

design is “best;” there are strengths and weaknesses of each. The most appropriate and valid study design varies based on the research question being asked.

Experience as a Medical Expert

For the National Academy of Medicine, I have contributed to several reports, including Saving Women’s Lives (2004), Improving Mammographic Quality Standards (2005), and Breast and the Environment: A Life Course Approach (2012), for which I wrote a review on the association between radiation exposure and breast cancer (Appendix). In addition to this research, I am actively involved in raising awareness of the need for better standards and greater safety around medical imaging, in particular related to radiation exposure. I have spoken at the US Food and Drug Administration, testified before the US Congress on several occasions, and worked with leading professional societies to focus attention on improving medical imaging safety. I have written several quality measures on radiation dose adopted by the National Quality Forum and developed educational tools to help physicians and patients understand the importance of minimizing radiation exposure from imaging.

Prior to providing my opinions on the association between talcum powder products and ovarian cancer, I had not reviewed the relevant literature and had not published in this area. As a result, I brought an unbiased perspective to my review. This report reflects my review of medical and scientific publications in this area (overviews and scientific studies), my own analysis, and review of documents shared with me by the lawyers who engaged me for this task. My curriculum vitae is attached as Exhibit A, the materials I considered are attached as Exhibit B, and my fees and prior testimony are attached as Exhibit C.

III. Background: Ovarian cancer and Talc as a Modifiable Risk Factor

Ovarian Cancer

Ovarian cancer is the seventh most common cancer in women and the fifth leading cause of cancer deaths in the United States.¹ In 2018, 22,240 women are expected to receive a new diagnosis of ovarian cancer and 14,070 women will die from it. Overall, about 1 in 78 women (1.3%) will be diagnosed with ovarian cancer in their lifetime and around 1 in 108 will die of it. About 224,940 women are currently living with ovarian cancer.² Most cases occur among older women; the median age at diagnosis is 62, although this varies by ovarian cancer type.² Ovarian cancer is frequently diagnosed at a late stage, when a cure is unlikely. Because so many ovarian cancers are diagnosed at a late stage, the overall mortality rate is high, and the overall 5-year survival is poor. With the poor prognosis and absence of a reliable screening test to find ovarian cancer early, it is a highly feared cancer for women and their physicians alike.

Histologic types

Cancers are classified by histologic type, meaning the type of cells that are involved. Understanding ovarian cancer histologic types is important because the risk factors, etiology and genetics of ovarian cancer can vary by histological type. Therefore, the importance of talcum powder products as a risk factor or cause can also vary by type.

Ovarian cancers (epithelial and non-epithelial) are a heterogeneous group of malignancies that vary in their pathological appearance, molecular biology, risk factors, etiology and prognosis.¹ Epithelial ovarian cancers have several histologic types; most fall into a small group of more common types including serous, endometrioid, clear cell and mucinous. About 90% of ovarian cancers are epithelial (meaning they arise from cells on the surface of the ovary or fallopian tube) and the most common type of epithelial cancer is serous carcinoma. Serous is not only the most common type of ovarian cancer, it is also the most lethal type of ovarian cancer. Further, it is the type of cancer that pathologists can most consistently, reliably, and reproducibly diagnose. Thus, epidemiological studies will have the greatest ability to document a clear association between serous ovarian cancer types and talcum powder products, if a connection exists. It is also the subtype that has been studied most from a molecular and pathologic research standpoint.

Table 1. Histologic Types of Ovarian Cancers Diagnosed Over 15 Years at the KP Washington (in press, JAMA Internal Medicine)		
Histologic Type	Number	Percent of Total Cancers
Papillary serous cystadenocarcinoma	52	36.6
Endometrioid carcinoma	17	12.0
Serous cystadenocarcinoma	15	10.6
Clear cell adenocarcinoma	12	8.5
Adenocarcinoma, NOS	11	7.7
Mucinous adenocarcinoma	7	4.9
Mixed cell adenocarcinoma	3	2.1
Serous surface papillary carcinoma	3	2.1
Granulosa cell tumor	3	2.1
Carcinoma, not otherwise specific	2	1.4
Mucinous cystadenocarcinoma	2	1.4
Mucinous cystic tumor of borderline	2	1.4
Carcinoma in situ	1	0.7
Squamous cell carcinoma	1	0.7
Papillary adenocarcinoma	1	0.7
Papillary serous cystadenoma, borderline	1	0.7
Adenocarcinoma with squamous meta	1	0.7
Granulosa cell tumor, malignant	1	0.7
Endometrial stroma sarcoma	1	0.7
Mullerian mixed tumor	1	0.7
Carcinosarcoma	1	0.7
Carcinosarcoma, embryonal	1	0.7
Teratoma, malignant	1	0.7
Astrocytoma	1	0.7
Marginal zone B-cell lymphoma	1	0.7
Total	142	100
Summary		
Serous carcinoma	70	49.3
Endometrioid carcinoma	17	12.0
Clear cell carcinoma	12	8.5
Mucinous carcinoma	9	6.3

My research group recently reported on the ultrasound appearance of ovarian cancers among a large cohort of women. The purpose of this cohort study was to quantify the risk of malignant ovarian cancer based on ultrasound findings. We described 142 new ovarian cancer cases in a population of 500,000 women enrolled in Kaiser Permanente Washington, an integrated health plan, between 1997 and 2008, including 72,093 women who underwent pelvic ultrasound. The distribution of cancer histological types is in Table 1. Serous carcinoma was the most common cancer type: In our cohort, it was 50% of the ovarian cancers. Serous carcinoma has the worst prognosis of the ovarian cancer types. Its high frequency and poor

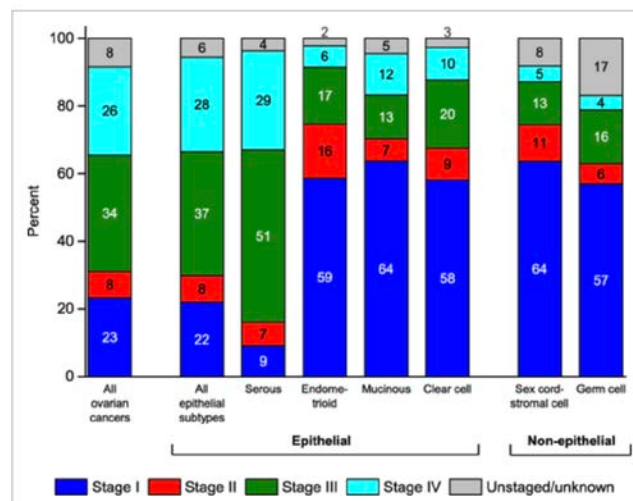
prognosis contribute to the high mortality rate for ovarian cancer overall. The other common histological types of ovarian cancer were endometrioid (12% in our data), clear cell (8.5% in our data), and mucinous (6.3% in our data).

Ovarian cancer types have large differences in stage of diagnosis (a strong predictor of survival) and prognosis independent of stage. The 5-year survival by histological type is in Table 2. Serous cancer is the most frequent and most aggressive, with an overall 5-year survival of 43% as compared with 82% for endometrioid. The survival is strongly influenced by stage at diagnosis, with higher stage numbers indicating more advanced stage.¹ Most serous carcinomas are diagnosed at stage III (51%) or IV (29%) (Figure 1),² for which 5-year survivals from the most recent data were 42% and 26%, respectively. These data reflect the aggressive nature of serous cancer.¹ In contrast, the majority (58% to 64%) of endometrioid, mucinous, and clear cell carcinomas are diagnosed at stage I, similar to nonepithelial tumors (Figure 1). Consequently, the 5-year survivals are 82%, 71%, and 66%, respectively, for endometrioid, mucinous, and clear cell carcinoma. Thus, these cancers behave very differently, even though all are ovarian epithelial cancers.

Table 2. Percent of Women Surviving 5 Years After Diagnosis by Epithelial Ovarian Cancer Type. Data From 2008–2013.

	All epithelial types	Serous	Endometrioid	Mucinous	Clear cell	Sex cord-stromal	Germ cell
Stage							
All	47	43	82	71	66	88	94
Stage I	89	86	95	92	85	98	99
Stage II	71	71	84	69	71	84	93
Stage III	41	42	59	30	35	61	90
Stage IV	20	26	29	13	16	41	69

Figure 1. American Joint Committee on Cancer Sixth Edition Stage Distribution (%) for Ovarian Cancer by Histology, US, 2007-2013, SEER 18 Registries, NCI, 2017. This shows that serious cancers are more likely to be diagnosed at state III, IV (green and teal), compared with other tumor types.



This summary reflects our current knowledge about ovarian cancer histologic types and their associated prognoses. As research results are reported, our knowledge will evolve. For example, recent studies suggest we need to improve our ability to distinguish between high-grade serous and endometrioid carcinomas. Other results suggest that many ovarian mucinous carcinomas are actually gastrointestinal tumors that metastasized to the ovaries and this realization is affecting the reported rates of ovarian mucinous carcinomas (which are declining).^{1,3,4} The categorization of noninvasive tumors classified as borderline is also under investigation and a topic of discussion in the field. These noninvasive tumors have historically been considered in the spectrum of ovarian cancer that have less aggressive behavior. However, many previously described borderline cancers are now generally considered non-malignant.

In summary, when assessing the carcinogenicity of talcum power products, this should focus on invasive serous carcinoma as the most important cancer (based on prognosis) and the most reliable cancer to identify (based on histology and understanding of cancer behavior).

Additionally, over the last decade, there has been research suggesting that many ovarian cancers originate from cells in the distal portion of the fallopian tube. Because the pathogenesis, treatment, and prognosis of serous cancers of the fallopian tube, ovary, and peritoneum are similar, these are now typically considered as a single entity.⁴ This consideration applies to the association with talcum powder product usage discussed in this report.

Risk Factors

Understanding ovarian cancer risk factors is important because analyzing the impact of talcum powder products exposure must consider *covariates, or other characteristics* that a woman might have that might also influence her ovarian cancer risk such as age, inherited genetic mutations, reproductive factors, or family history of cancer. Every risk factor does not have to be considered to come to a valid conclusion; indeed, this is not realistic within the limitations of medical research, and the bias introduced by the exclusion of some risk factors will be small. However, crude analyses that look at the risk of ovarian cancer from talcum powder products without adjusting for any other risk factors must be considered cautiously. For that reason, statistical analyses of research results often adjust for *confounding factors or variables that are covariates that hinder accurate calculation of an association*, for example between talcum powder products and ovarian cancer.

Numerous risk factors are identified for ovarian cancer.⁵ Unfortunately, few can be modified by therapies or lifestyle changes. Risk factors vary by histologic type⁵ but those that increase risk of ovarian cancer include personal or family history of ovarian or breast cancer, inherited mutations including BRCA1 and BRCA2⁶⁻¹⁰ advanced age, white race, increased education, and endometriosis. Other factors that may increase ovarian cancer risk due to estrogen exposure include having no pregnancies or advanced age at first birth, obesity, and postmenopausal hormone therapy.¹¹⁻¹³ Several factors are associated with reduced risk for ovarian cancer including breast feeding, multiple pregnancies, use of oral contraception,

tubal ligation, and removal of uterus, fallopian tubes, or both. ¹⁴⁻¹⁸ Smoking is a possible risk factor for ovarian cancer, primarily mucinous subtype, although study results have not been consistent. ^{5,19}

Risk factors vary by cancer type. For example, serous cancer is more strongly associated with reproductive risk factors than mucinous tumors ²⁰⁻²² and different histologic types have different molecular and genetic profiles. ²³⁻²⁵ Serous tumors are more likely to have a cancer-promoting mutation in the p53 gene, whereas similar KRAS mutations are more common in mucinous tumors. Over time, the occurrence of ovarian cancer has changed, in part due to changes in risk factors. For example, small declines in the rates of endometrioid and serous cancer are attributed to declining use of hormone replacement among postmenopausal women.

Etiology: Origins, Causes, Development and Inflammation

Our understanding of the etiology and course of ovarian cancer continues to evolve. Hereditary genetic predisposition increases risk, but overall, accounts for only a small proportion of cancers. And even in women with hereditary genetic mutations, not all will develop ovarian cancer. The majority of ovarian cancers are now believed to arise in the distal portion of the fallopian tube. By convention, fallopian tube, ovary and peritoneal cancers are considered as a single entity. The most widely accepted mechanism for initiation, promotion and progression of ovarian cancer is tissue inflammation leading to a series of responses that result in cancer.

There is very clear and extensive scientific literature describing the relationship between inflammation and cancer across many anatomic areas. Chronic inflammation, and even subtle, subclinical inflammation, is associated with an increased risk of cancer. ²⁶⁻²⁸ Many inflammatory conditions predispose to cancer development. Diverse factors that lead to inflammation - infection, chemical exposures, physical agents, autoimmune factors, and even inflammatory reactions of uncertain etiology - can lead to an increase in cancer incidence. For example, there are well described and accepted causal pathways linking inflammation in the etiology of bladder cancer (schistosomiasis, toxic chemicals), cervical cancer (papillomavirus), gastric cancer (H Pylori), colon cancer (inflammatory bowel disease), liver cancer (hepatitis), mesothelioma (asbestos) and ovarian cancer (pelvic inflammatory disease and endometriosis). The biological pathways associated with inflammation include stimulation/interference with a range of biological responses that are involved in initiation of cancer, promotion of cancer, and progression of cancer. Oxidative stress resulting from inflammation can impact all stages of cancer development including cancer initiation (DNA is damaged by introducing gene mutations and structural alterations of DNA leading to inhibition of DNA repair and malignant transformation); promotion (which may be manifest as abnormal gene expression resulting in cell proliferation and decrease apoptosis) and progression (further DNA damage and enhancement of cell growth. ²⁹ Local inflammatory response can lead to signaling molecules such as cytokines, chemokines, prostaglandins, growth transcription factors, microRNAs having higher expression that can promote cancer

development and can create a favorable microenvironment for the development and progression of cancer.³⁰ Inflammation impacts every step of tumorigenesis, from initiation through tumor promotion, and extending to metastatic progression. Similarly, the most compelling mechanism for the etiology of ovarian cancer is that of chronic inflammation and scarring in the ovary that leads to malignant transformation and cancer progression. This mechanism involves cell proliferation, oxidative stress, DNA damage and gene mutations.³¹⁻³³ The microenvironment of ovarian cancer contains a broad spectrum of pro-inflammatory cytokines and chemokines contributing to the mechanism.³⁸

There are many processes that can lead to inflammation and tumorigenesis and the exposure to talcum powder products is one such exposure that can strongly enhance the tumor promotion or progression as seen in in vitro and animal studies. For example, normal repeated ovulation leads to injury of ovarian epithelial cells and transformation to malignant cancer cells that can be enhanced by various factors such as talc or asbestos particles. Exposure to talcum powder products can induce the production of pro-oxidant enzymes and reduced production of antioxidant enzymes leads to malignant transformation. In support of inflammation from talcum powder products causing cancer, hysterectomy or bilateral tubal ligation, which would significantly limit ovarian exposure to inflammatory mediators, and toxins, is associated with reduced ovarian cancer risk.

Relationship Between Ovarian Cancer and Talcum Powder Products

The epidemiological evidence described in detail below demonstrates a strong and positive association between exposure to talcum powder products and ovarian cancer and that talcum powder products cause ovarian cancer. Although epidemiologic evidence alone does not provide a definitive mechanism or pathophysiological process that accounts for the increased risk, the evidence for inflammation as described above is very strong. Similarly, epidemiological evidence alone does not confirm the specific component or ingredient in talcum powder products that is responsible for its carcinogenesis. Nonetheless, several constituents within talc powder products are worth highlighting as they may be acting individually or together to create the carcinogenicity of talc powder products inasmuch as they are individually highly carcinogenic

Why Talcum Powder Products were Initially Suspected as Causing Ovarian Cancer

In 1978 samples of commercial body powders were shown to contain asbestos silica minerals. Asbestos was a known carcinogen and about half of the powder samples contained respirable quartz, a lung carcinogen. Concerns were primarily raised that inhaled powder could cause lung scarring, lung cancer, or mesothelioma. In 1971, Henderson observed talc particles deeply embedded in ovarian cancer tissue. The authors noted the close association of talc to the asbestos group of minerals.³⁹ Further concern was raised, in 1982 when a case-control study of ovarian cancer that collected information on talcum powder use reported an increased risk with perineal dusting.⁴⁰ These findings were reported in widely circulated newspapers such as The Globe, raising concern that the powders were carcinogenic because

of the contamination with asbestos, using the relationship between asbestos and lung cancer and mesothelioma as the basis for the concern.

Carcinomic of Constituents of Talc Powder Products

There are hundreds of different constituents and ingredients within talcum powder products in addition to platy talc. Many of these are Group 1 carcinogens (such as asbestos, talc containing asbestiform fibers, heavy metals, and some fragrance chemicals) that likely contribute to the carcinogenicity of the products.

Asbestos

Asbestos is the generic commercial designation for a group of naturally occurring mineral silicate fibers; serpentine mineral fibers are called chrysotile, and amphibole minerals include actinolite, amosite, anthophyllite, crocidolite and tremolites. Talc is formed by complex geological processes acting on pre-existing rock formations with diverse chemical composition. Small amounts of chrysotile (asbestos) may occur in these talc deposits ^{41,42} When talc is mined it may contain asbestos fibers ^{42,43} A study of 21 consumer talcum powders obtained from retail stores in 1971–1975 reported that 10 contained concentrations of asbestos fibers ranging from 0.2 to 14%. ^{41,44} Because of concern that asbestos was present in talcum powder products and the known carcinogenicity of asbestos, it has been reported that voluntary guidelines were established by the cosmetic industry in 1976 to limit the content of asbestos fibers in commercial talc preparations. While currently talcum powder products are believed to be free from asbestos, the data on its continued presence are strong. I have seen evidence of continued presence since 1976. ⁴⁵⁻⁴⁸ For example, Longo tested approximately 50 samples that were taken between the years 1960 through 2000 and the majority of sample are positive for asbestos. ⁴⁷

Asbestos is a known and potent human carcinogen. Asbestos is highly carcinogenic to the lungs, lining of the lungs, and larynx. ⁴⁹ Asbestos is also highly carcinogenic to the ovaries. ⁴⁹⁻⁵⁸ Women working in asbestos-manufacturing industries have an increased risk of ovarian cancer. IARC reviewed the association between asbestos exposure and ovarian cancer in 2012. To assess the relationship, IARC reviewed data primarily from large epidemiological cohort studies of women who had occupational exposure to asbestos as well case-control studies on non-occupational exposure. The context and lengths of exposures varied, along with the type of asbestos fibers to which the women were exposed and the study designs and assessments. Nonetheless, the results were consistent. Most, but not all, were statistically significant and documented a strong and compelling causal association between exposure to asbestos and ovarian cancer, largely the result of the association from cohort studies of women with substantial occupational exposures. ⁵⁰⁻⁵⁴ **IARC concluded that there is sufficient evidence that asbestos is carcinogenic in humans and that asbestos causes cancer of the ovary.** This is the highest risk category. ⁴⁹ IARC also concluded that this categorization applied to all forms of asbestos and to talc containing asbestiform fibers (talc in a fibrous habit or fibrous talc)). IARC also concluded that asbestos is carcinogenic based on animal studies. Camargo completed a systematic review of the relationship between women occupationally exposed to asbestos and ovarian cancer. ⁵⁹ The authors found that of the 18 cohort studies

the pooled standard mortality estimate for ovarian cancer was 1.77 (95% confidence interval, 1.37-2.28). The range in reported SMR values was 1.1– 5.4 across the included cohort studies and the most common values were 2–3. This study supports IARC's conclusion that exposure to asbestos causes ovarian cancer.

IARC explicitly stated that the findings in this Monograph applied to all forms of asbestos, as well as asbestiform talc (fibrous talc).

I reviewed many publications and primary research studies, including experimental and basic science models showing molecular and genetic cancer-promoting changes to cells that occur from exposure to asbestos fibers. I also strongly conclude that asbestos causes ovarian cancer.

Talc

Talc is the primary component of talcum powder products. The chemical structures of talc and asbestos can be similar. While talc particles are usually plate-like, talc can also grow as a fiber which is similar to the group of minerals called asbestos. Both are magnesium silicate and when talc has the fibrous form it is called asbestiform because of its similarity to asbestos. The form of the talc fibers is long and thin, with parallel bundles that are easy to separate from each other, and closely resembles the physical appearance of asbestos minerals. The histologic appearances of mesothelioma and ovarian cancer are similar. The known carcinogenicity of asbestos for lung, pleural, peritoneal and ovarian cancer has led to the theory that the similarity in the fibers and the resulting cancers suggests that talc works mechanistically within the ovary to induce cancer in a way that is similar to how asbestos in the chest induces mesothelioma.

Early observations demonstrated talc particles in both malignant and normal ovaries establishing a route from the perineum to the ovary and shows that many women are exposed to talc.^{39,60} In 2006, the International Agency for Research on Cancer (IARC) reviewed the data on cosmetic (perineal) talc ("non-asbestiform") application and concluded that it is possibly carcinogenic to humans.⁶¹ This is not as strong a recommendation as they made for asbestos and ovarian cancer, but nonetheless is a strong recommendation. IARC classified genital-perineal use of talc-based powder as possibly carcinogenic. Exposure to talc particles can induce an inflammatory response, either directly at the ovary and ovary-fallopian tube juncture, causing local irritation from talc particulates or through more generalized peritoneal inflammation. The mechanism that can lead to cancer is local irritation by talc fibers that disrupts the epithelial surface, increasing rates of cell division and DNA repair that can lead to mutations. Also increased are oxidative stress and cytokine production, indicating inflammation. Fibers that are incorporated into the epithelial cells enter ovarian tissue. This inflammation initiates a series of responses, supported by research, that promote cancer. The reduction in the elevated risk of ovarian cancer from talcum powder exposure after hysterectomy or tubal ligation supports the mechanism by which local irritation and inflammation to the ovary from talc or asbestos causes an elevated cancer risk.

Heavy Metals

Talc powder products can contain Group 1 metals that are considered by IARC as carcinogenic to humans.^{44,49}

This includes nickel compounds which IARC documents cause lung and nasal cavity and paranasal sinus cancer. (IARC100c-10, 2012). Nickel compounds “cause DNA damage, chromosomal aberrations, delayed mutagenicity and chromosomal instability ... and nickel compounds act as co-mutagens.” Talcum powder products also contain Chromium (VI) (IARC100c-9, 2012) another Group 1 carcinogen, where there is sufficient evidence in humans for carcinogenicity (to the nose and nasal sinus). The mechanism includes “DNA damage, generation of oxidative stress and aneuploidy. Talc powder products can also contain Group 2A metals that are considered probably carcinogenic to humans, such as Cobalt which can be found in talc powder products.⁶² IARC considers Cobalt metal with tungsten carbide as probably carcinogenic to humans (Group 2A), but worth noting that a number of the IARC working group members supported an evaluation in Group 1 because they judged the epidemiological evidence to be sufficient, leading to an overall evaluation in Group 1; or they judged the mechanistic evidence to be strong enough to justify upgrading the default evaluation from 2A to 1. The majority of working group members, who supported the group 2A evaluation, cited the need for either sufficient evidence in humans or strong mechanistic evidence in exposed humans. Cobalt metal without tungsten carbide is also considered possibly carcinogenic to humans (Group 2B). Cobalt sulfate and other soluble cobalt(II) salts are possibly carcinogenic to humans (Group 2B).

Any and all of these heavy metals can cause ovarian cancer through an inflammatory mechanism

Fragrances

There are more than 150 different chemicals added to Johnson’s Baby Powder and Shower to Shower products. I reviewed the expert report from Dr. Crowley that concludes that some of these chemicals may contribute to the inflammatory response, toxicity, and potential carcinogenicity of Johnson & Johnson’s talcum powder products. I concur with his opinion.⁶³

IV. Overview of Publications on Genital Use of Talc Powder Products and Ovarian Cancer

To understand the relationship between exposure to talcum powder products and ovarian cancer, I searched for and reviewed scientific papers on this topic. I used several searchable publication databases (Scopus, Embase, Pubmed) and manually searched the reference lists of all articles I found, including a large number of reviews. The results of my review follow the explanation of the main types of studies and articles.

Explanation of study designs and article types

Nearly all published studies that I reviewed used one of two designs: case-control and cohort. Each design has strengths and biases. The commonly held view is that cohort studies are better than case-control studies. This is a misconception thus it is worth explaining their differences. Many articles I reviewed were systematic reviews, which are also explained.

Case-control studies compare people with a condition (cases) by matching them to people with similar characteristics who do not have the condition (controls) to determine the effect of a potential disease-causing factor. They often analyze existing data retrospectively, after people have been diagnosed, and involve tens or hundreds of patients. Cohort studies compare cohorts, or groups of people, who were exposed or not exposed to a potential disease agent. They often collect data on people prospectively, before they develop a disease and track their health over time. Both case-control and cohort studies, if well done, can provide accurate and meaningful information about statistical associations. In general, however, the risk of bias is greater for case-control studies. (An example is recall bias, in which women are more likely to remember and report exposure to talc powder products after they have been diagnosed with cancer compared to women without a diagnosis, perhaps because diagnosed women heard that talc powder products is harmful and are more likely to remember talc use). Nonetheless, when studying a rare disease, the case-control design is frequently highly efficient and desirable as it allows you to assemble a much larger number of cases and can delve in great depth for particular exposures. You can identify all patients who have the outcome of interest, and then query them (and some control group) about any antecedent exposure. The identification of the control group is very important. My large, National Institutes of Health-funded study of cancer risk factors in children is employing a case-control design. This design permits us to ask very detailed questions of a small number of individuals about their various exposures.

Cohort studies potentially avoid some biases of case-control studies since exposures are prospectively assessed and quantified, that is, before disease outcomes. This design also has limitations, though. An extremely important limitation is that because cohort studies are expensive and time-consuming, they rarely focus on a single, narrowly defined question such as the association between regular use of talcum powder products and cancer. Usually, researchers investigate a broad range of questions in cohort studies, so asking patients in-depth questions about any given topic is difficult, especially since tens of thousands of patients may be surveyed on many topics. Further, in cohort studies, having comprehensive assessment of outcomes on all individuals in the cohort is extremely important. Losing patients to follow up (meaning researchers cannot contact or find records on a participant) leads to study bias. The other disadvantage of cohort studies is that a very large number of patients must be assessed over a long period of time to see who will develop a rare outcome (like ovarian cancer). Because of this, typically there will be far fewer patients with disease in a cohort study as compared with case control study (like in this case).

The small number of cohort studies I found on the relationship between talcum powder products exposure and ovarian cancer did not focus on the details of this topic. While they may have included questions about talcum powder exposure, they were not sufficiently nuanced to provide meaningful information. Thus, in most of the cohort studies I found, measurements of exposure were poor, not specific, or inaccurate. Further, several had very short follow-up periods with data or information about the time before the cancer occurred. This negates an advantage of cohort studies, which is being able to learn about exposures before the cancer, eliminating recall bias.

Systematic reviews quantitatively summarize results across multiple studies. One of the rationales of this study design is that individual studies may not have enough participants to yield meaningful results because they are too small or insufficiently powered. Combining small studies can provide more stable and reliable summary estimates of the effects of disease agents and risk factors. Further, a systematic review may be better than a single study, as it provides broader evidence of the results and includes patients from diverse settings. However, in order to statistically combine and summarize the data from different research studies into a single systematic meta-analytic review, the combined studies must ask the same research question and follow sufficiently similar and rigorous scientific methods. A meta-analysis does not compensate for gaps or flaws in an original study: Combining three poorly performed studies does not yield reliable summary estimates even though there may be three times the number of patients. Similarly, combining studies that ask different research questions (for example, assessing women of different ages for a disease in which age is an important risk factor) does not provide reliable summaries. Results from different studies often vary when the studies ask different research questions, have different criteria for including participants, or use different methods. I raise these issues to point out that systematic reviews must be read extremely carefully to ensure that their conclusions are valid.

Table of Reviewed Publications

I identified and reviewed 43 English-language publications that provided quantitative data based on epidemiological studies about the relationship between genital talcum powder exposure and ovarian cancer (Table 3). This list includes 4 cohort studies, 8 systematic meta-analytic reviews, 2 studies that pooled individual patient-level data from several research studies, and 30 case-control studies. One study contributed both the systematic review and a case control study. I also read multiple review articles that are not included in the table. The epidemiological studies were published between 1982 and 2018. I have described the results organized by study design below.

Most studies used a case-control study design with a small number using a cohort study design. Although some studies assessed powder use to any part of the body or assessed the use of talcum powder on diaphragms, condoms or sanitary napkins, the primary research question that I focused on in my review and that was assessed in all included individual research studies, was whether genital area exposure to talcum powder increases risk of epithelial ovarian cancer. Occasionally, study authors assessed combination exposures (i.e., to genitals and other body parts). These studies were included as long as genital powder use was assessed. Nearly all studies adjusted for known ovarian cancer risk factors, but those factors varied. The vast majority of studies found a positive association between any exposure to talcum powder products and cancer. However, the sample size of some studies was small and resulted in high statistical uncertainty. Because of these and other limitations, quantifying a precise association between exposure and cancer was difficult from my review of the literature. The data for some studies may have shown that effects of talcum powder exposure (measured as odds ratios, ORs) was meaningful for cancer development, but with statistical

uncertainty; whereas other studies showed the reverse results, with ORs not showing a positive association, but statistical parameters suggesting that a meaningful association was nonetheless possible because of wide confidence intervals. Therefore, I thought a more precise and careful review was called for. The number of individual women included in each study and the reported or estimated effect size for “any exposure to talc” (adjusted for other risk factors such as age) are in Table 4.

A subset of the studies quantified the *intensity (frequency)* of each woman’s exposure to talc to assess the importance of use patterns (e.g., if a single lifetime use or weekly, monthly, or daily use increased ovarian cancer risk) or *dose dependency (links between the number of exposures and cancer risk, e.g., if doubling exposure doubles risk)*. Further, a subset of studies stratified by cancer type (invasive vs. low malignant potential/borderline) and whether the risks varied by histological types including the four dominant types of serous, mucinous, clear cell, and endometrioid cancer.

Studies that provided data on the frequency of talc use and association by histologic type were included in a separate systematic meta-analytic review that I conducted as part of my review of the literature to include in this report. The reason I completed my own statistical review is further explained below.

Quantifying Exposures

A large proportion of women will have used talcum powder products, highlighting the importance of this issue. However, publications that focus on women reporting “any” genital exposure to talc (i.e., talc at any point in life and for any duration) may be too broad to provide meaningful information. For example, “any use” will include women who applied talc powder products three times over five decades and women who used talc powder products daily, whose might have had 20,000 applications and exposures in comparison to three. Defining a variable as any use is the equivalent to creating a variable of any smoking use, that combines data on individuals who tried one cigarette in their life with individuals with 50 pack years of tobacco use. Combining data on women with infrequent or sporadic exposures with data from women with frequent, sustained use leads to imprecise results, masking any causal associations. Therefore, I selected the studies for my own review that quantified the frequency of talc powder products use as having the most informative data and included them in a separate systematic review.

Summary of Data

I grouped the research studies by their study design. What follows is my review of the cohort studies, systematic review studies, pooled data studies, followed by my own review.

Cohort Studies

Four cohorts (Gertig, Gates, Houghton, Gonzalez) have been published on talcum powder products and ovarian cancer.

Cohort 1: Gertig (2000) ⁶⁴

This first cohort study assessed the relationship between perineal talc and ovarian cancer within the context of the US Nurses' Health Study, a prospective study of 121,700 female registered nurses in the United States who were aged 30–55 years at enrollment in 1976. These are mostly premenopausal women. While talc exposure was not an initial part of the study, questions about talc, including measuring frequency of exposure, were added in 1982; a large subset of the cohort (78,630 women) completed these questions and were included in analyses. Among these women who were followed for 14 years, 307 were diagnosed with epithelial ovarian cancer. After adjusting for confounding variables, the *relative risk (RR)* of developing ovarian cancer (*the likelihood of ovarian cancer in talc users compared to nonusers, with higher RR meaning increased risk stronger association*) among daily users of talc was RR 1.12 (95% confidence interval [CI] 0.82, 1.55, *a measure of statistical uncertainty, with wider ranges indicating greater uncertainty*), which was not statistically significant. However, when results were classified by histologic subtype, the RR of invasive serous cancers was significantly elevated among any users of talc (RR 1.40, 95% CI 1.02, 1.9) and the RR of invasive serous cancer among daily users of talc was higher at RR 1.49 (95% CI 0.98, 2.3).

In this cohort study, the researchers assessed talc exposure before cancer diagnosis, avoiding the possibility of the recall bias of case-control studies. This was a strong strength of this study. A potential weakness was that frequency (i.e. daily) but not duration (number of years) of talc use was measured, so a clear lifetime exposure measure was missing. The researchers nonetheless quantified exposure at the time the talc questions were asked, which was probably strongly associated with prior use (i.e. an approximation on ongoing use). **This study provides strong evidence that perineal exposure to talc increases the risk of invasive serous ovarian cancer, particularly among daily users of talc, with about a 50% increased risk,** which is substantial and meaningful.

Cohort 2: Gates (2010) ²⁴

This study assessed the association between ovarian cancer risk factors and incidence of ovarian tumors by histological type using data from the US Nurses' Health Study combined with data from the Nurses' Health Study II, which included a second period of enrolling participants. Unfortunately, talc use was assessed only on the first survey and not assessed among patients enrolled in the Nurses' Health Study II. Thus, this extends the period of follow up from the initial NHS but does not include greater information about risk factors. Results were presented for any talc powder products use and not for frequency of use. **Thus, this report does not add to a meaningful assessment of the relationship between talc use and ovarian cancer because it used exactly the same patient group as Gertig (2000) but provided less information to quantify the frequency of talc use.**

Cohort 3: Houghton (2013) ⁶⁵

This study assessed perineal talc powder products use and risk of ovarian cancer in the Women's Health Initiative Observational study, in which postmenopausal women aged 50–79 were enrolled in a prospective cohort of women from 40 clinical centers across the United

States in 1993–1998. Overall, 61,576 women were included in analyses, including 429 diagnosed with ovarian cancer. Perineal powder use was assessed at the start of the study. Participants were asked if they **ever used talc powder products** on their private parts (genital areas). Those who responded yes were asked about duration (years) of use. Women were followed for a mean of 12 years and the median age of participants was 63. **Talc powder products use was associated with a 12% increase in risk of ovarian cancer after accounting for covariates** (RR 1.12, 95% CI 0.92, 1.36). When limited to women who used perineal powder for 20 years or more, the RR was 1.10 (95% CI 0.82, 1.48). When limited to serous ovarian cancer, the RR was 1.13 (95% CI 0.84, 1.51.) **The primary limitation of the study was that frequency of talc powder products use was not assessed—and thus the authors could focus only on any talcum powder use.** The imprecision in estimation of talcum powder exposure makes the results not terribly meaningful. The second limitation was the relatively short follow-up of 12 years to identify ovarian cancer diagnoses.

Cohort 4: Gonzalez (2016) ⁶⁶

The Sister Study (2003–2009) followed 50,884 women ages 35 to 75 years in the US and Puerto Rico who had a sister diagnosed with breast cancer. After excluding participants who had bilateral oophorectomies, ovarian cancer, or were lost to follow-up, 41,654 participants were included. At baseline participants were asked about douching and talc use during the previous 12 months, and during follow-up (median of 6.6 years) 154 participants reported a diagnosis of ovarian cancer. The authors computed adjusted hazard ratios (HR) and 95% confidence intervals (CI) for ovarian cancer risk using the Cox proportional hazards model. The authors found no significant association between baseline perineal talc use and subsequent ovarian cancer (HR: 0.73 CI: 0.44, 1.2). **The primary limitations of this study are that the authors combined a large number of potential talc exposures into a single category, including genital talc use in the form of powder or spray applied to a sanitary napkin, underwear, diaphragm, cervical cap, or vaginal area. Further, the authors categorized the exposure based on the 12 months prior to enrollment as a dichotomous ever/never.** Thus not only was it an ever versus never category, the ever category was extremely broad, making the lack of association less meaningful. Further, there are several other factors that make the results questionable, including lower than expected proportion of women who report any exposure to talc powder products, and the lack of a validated approach to ascertainment of ovarian cancer.

Cohort Studies: Summary

Analyses of data from the US Nurses' Health study and the Women's Health Initiative estimated that women who report any exposure talc powder products will have a 12% increase in ovarian cancer compared to women who never report talc powder products use, although this estimate was not statistically significant. The primary limitation of this estimate is that it is based on *any talc powder products* use, which is a weak, crude predictor. Similarly, while the results from the Sisters study did not identify a significant association between talc powder products use and ovarian cancer, they too used a measure of ever use, and included a large number of different types of exposures that would not be expected to measure a single exposure. The most important and meaningful conclusion that I draw from the cohort studies

is from the Gertig 2000 study using data from the US Nurses' Health study: That women who are **daily users of talc have an approximately 50% increase (OR 1.49) in their risk of invasive serous** cancer, the most lethal and frequent type of ovarian cancer.

Systematic Reviews

I found nine systematic reviews that summarized the relationship between talc and ovarian cancer, summarized below. These reviews were completed using various subsets of the full list of publications. The systematic reviewers are presented with the most recent first, because the more recent studies tended to be more complete, comprehensive and the most methodologically rigorous.

Systematic Review 1: Penninkilampi (2018) ⁶⁷

This comprehensive systematic review of the association between any genital use of talcum powder products and ovarian cancer conducted a stratified analyses showing the association by frequency of talc use and histologic cancer subtype. The methods of the study are well described. The researchers identified studies using six electronic databases and reviewed publications with 50 or more cases of ovarian cancer. They identified 24 case-control studies describing 13,421 cases and the three cohort studies (890 cases, 181,860 person-years) described above. Any reported use of perineal talc powder products was associated with increased risk of ovarian cancer compared to no use (OR = 1.31; 95% CI 1.24, 1.39). Women with more than 3600 lifetime applications had slightly higher risks (OR = 1.42; 95% CI 1.25, 1.61). Women who reported long-term (>10 years) talc use also had an increased risk (OR 1.25; 95% CI = 1.10, 1.43). The association between any talcum powder product exposure and ovarian cancer was limited to studies that used a case-control design. The cohort studies showed an increased risk of serous invasive cancer subtypes for perineal talc use compared to no use (OR = 1.25; 95% CI = 1.01, 1.55). While serous and endometrioid cancer were associated with talcum powder products use, no association was seen with mucinous or clear cell cancers. The review authors concluded, from the data, that perineal talcum powder use and ovarian cancer were consistently associated, with a slightly higher risk in women who report greater usage. Some variation in the magnitude of the effect of talcum powder products was found when considering the study designs and ovarian cancer subtypes. Several small methodological issues are that Penniniklampi may have included some groups of patients more than once in analyses and did not include updated data or previously unpublished data available from a research consortium on ovarian cancer. However, these concerns are unlikely to have had a significant impact on their estimates.

Table 3. List of Included Studies, sorted by study design

	Study Type	Year	Author	Journal	Title
1	Cohort Study	2000	Gerting	J Natl Cancer Inst	Prospective study of talc use and ovarian cancer (in the Nurses' Health Study)
2	Cohort Study	2010	Gates	Am J Epidemiol	Risk factors for epithelial ovarian cancer by histologic type; US Nurses Health Study
3	Cohort Study	2014	Houghton	J Natl Cancer Inst	Perineal powder use and risk of ovarian cancer: Results from the Women's Health Initiative
4	Cohort Study	2016	Gonzalez	Epidemiology	Douching, talc use and risk of ovarian cancer: Results from the Sister Study
5	Systematic Rev.	1992	Harlow	Obst Gyn	Perineal exposure to talc and ovarian cancer risk
6	Systematic Rev.	1995	Gross	J Expo Anal Env Epid	A meta-analytical approach examining the potential relationship between talc exposure and ovarian cancer
7	Systematic Rev.	2003	Huncharek	Anticancer Res	Perineal application of cosmetic talc and risk of invasive epithelial ovarian cancer: a meta-analysis of 11,933 subjects from sixteen observational studies
8	Systematic Rev.	2007	Huncharek	Eur J Cancer Prev	Use of cosmetic talc on contraceptive diaphragms and risk of ovarian cancer: a meta-analysis of nine observational studies.
9	Systematic Rev.	2008	Langseth	J Epid Community Health	Perineal use of talc and risk of ovarian cancer.
10	Systematic Rev.	2010	IARC	IARC Monographs	IARC monographs on the evaluation of carcinogenic risks to humans: Carbon black, titanium dioxide, and talc
11	Systematic Rev.	2017	Berg	European J of Can Prev	Genital use of talc and risk of ovarian cancer: A meta-analysis
12	Systematic Rev.	2018	Penninkilampi	Epidemiology	Perineal talc use and ovarian cancer: A systematic review and meta-analysis.
13	Pooled Data	2013	Terry	Cancer Prev Res	Genital powder use and risk of ovarian cancer: a pooled analysis of 8525 cases and 9859 controls
14	Pooled Data	2016	Cramer	Epidemiology	The association between talc use and ovarian cancer- A retrospective case- control study two US states
15	Case-Control	1982	Cramer	Cancer	Ovarian cancer and talc: A case control study
16	Case-Control	1983	Hartge	JAMA	Talc and ovarian cancer
17	Case-Control	1988	Whittemore	Am J Epidemiol	Personal and environmental characteristics related to epithelial ovarian cancer. Exposure to talcum powder, tobacco, alcohol, and coffee
5	Case-Control	1989	Harlow	Am J Epidemiol	A case-control study of borderline ovarian tumors: The influence of perineal exposure to talc
18	Case-Control	1989	Booth	BR Cancer	Risk factors for ovarian cancer: a case-control study
19	Case-Control	1992	Harlow	Obstet Gynecol	Perineal exposure to talc and ovarian cancer risk
20	Case-Control	1992	Rosenblatt	Gynecol Oncol	Mineral fiber exposure and the development of ovarian cancer
21	Case-Control	1992	Chen	Int J Epidemiol	Risk factors for epithelial ovarian cancer in Beijing, China
22	Case-Control	1993	Tzonous	Int J Cancer	Hair dyes, analgesics, tranquilizers and perineal talc application as risk factors for ovarian cancer
23	Case-Control	1995	Purdie	Int J Cancer	Reproductive and other factors and risk of epithelial ovarian cancer: an Australian case-control study
24	Case-Control	1996	Shushan	Fertil Steril	Human menopausal gonadotropin and the risk of epithelial ovarian cancer
25	Case-Control	1997	Chang	Cancer	Perineal talc exposure and risk of ovarian carcinoma
26	Case-Control	1997	Cook	Am J Epidemiol	Perineal powder exposure and the risk of ovarian cancer
27	Case-Control	1998	Green	Int J Cancer	Tubal sterilization, hysterectomy and decreased risk of ovarian cancer.
28	Case-Control	1998	Godard	Am J Obstet Gynecol	Risk factors for familial and sporadic ovarian cancer among French Canadians: A case-control study
29	Case-Control	1999	Cramer	International J of Cancer	Genital talc exposure and risk of ovarian cancer
30	Case-Control	1999	Wong	Obstet Gynecol	Perineal talc exposure and subsequent epithelial ovarian cancer: A case-control study
31	Case-Control	2000	Ness	Epidemiol	Factors related to inflammation of the ovarian epithelium and risk of ovarian cancer
32	Case-Control	2004	Pike	Fertil Steril	Hormonal factors and the risk of invasive ovarian cancer: A population based case control study
33	Case-Control	2004	Mills	Am J Epidemiol	Perineal talc exposure and epithelial ovarian cancer risk in the Central Valley of California
34	Case-Control	2008	Goodman	Endocr Relat Cancer	Association of two common single-nucleotide polymorphisms in the CYP19A1 locus and ovarian cancer risk
35	Case-Control	2008	Gates	Cancer Epid Bio Prev	Talc use, variants of the GSTM1, GSTT1, and NAT2 genes, and risk of epithelial ovarian cancer
36	Case-Control	2008	Merritt	Int J Cancer	Talcum powder, chronic pelvic inflammation and NSAIDs in relation to risk of epithelial ovarian cancer
37	Case-Control	2009	Moorman	Am J Epidemiol	Ovarian cancer risk factors in African-American and white women
38	Case-Control	2009	Wu	Int J Cancer	Markers of inflammation and risk of ovarian cancer in Los Angeles County
39	Case-Control	2011	Rosenblatt	Gynecol Oncol	Mineral fiber exposure and the development of ovarian cancer
40	Case-Control	2012	Lo-Cignaia	Epidemiol	Aspirin, non-aspirin non-steroidal anti-inflammatory drugs, or acetaminophen and risk of ovarian cancer
41	Case-Control	2012	Kurta	Cancer Epid Bio Prev	Use of fertility drugs and risk of ovarian cancer: results from a U.S.-based case-control study
42	Case-Control	2015	Wu	Cancer Epid Bio Prev	African Americans and Hispanics remain at lower risk of ovarian cancer than non-Hispanic whites after considering nongenetic risk factors and oophorectomy rates
43	Case-Control	2016	Schildkraut	Cancer Epid Bio Prev	Association between body powder use and ovarian cancer: the African American Cancer epidemiology Study

Table 4. List of Included Studies with Number of Cancers, Controls, and Reported Odds Ratios

	Study Type	Year	Author	Cancers	Controls or Cohort Size	Odds Ratio	95% CI
1	Cohort Study	2000	Gerting	307	78,630	1.12	(0.82,1.55)
2	Cohort Study	2010	Gates	797	108,073	1.06	(0.89, 1.28)
3	Cohort Study	2014	Houghton	427	61,576	1.12	(0.92,1.36)
4	Cohort Study	2016	Gonzalez	154	41,654	0.73	(0.44,1.2)
5	Systematic Review	1992	Harlow *	1,106	1,756	1.30	(1.1, 1.6)
6	Systematic Review	1995	Gross	1,333	2,362	1.29	(1.02, 1.63)
7	Systematic Review	2007	Huncharek	1,858	2,830	NA	NA
8	Systematic Review	2003	Huncharek	5,260	6,673	1.33	(1.16, 1.45)
9	Systematic Review	2008	Langseth			1.35	NA
10	Systematic Review	2010	IARC			1.30	
11	Systematic Review	2017	Berg	15,230	NR	1.22	(1.13, 1.30)
12	Systematic Review	2018	Penninkilampi	14,311	NR	1.31	1.24, 1.39
13	Pooled Data	2013	Terry	4,472	6,175	1.37	(1.19-1.58)
14	Pooled Data	2016	Cramer	2,041	2,100	1.38	(1.01,1.99)
15	Case-Control Study	1982	Cramer	215	215	1.58	(0.98, 2.47)
16	Case-Control Study	1983	Hartge	135	171	2.50	(0.70, 10.0)
17	Case-Control Study	1988	Whittemore	188	539	1.45	(0.94, 2.22)
5	Case-Control Study	1989	Harlow	116	158	1.10	(0.70,2.1)
18	Case-Control Study	1989	Booth	235	451	1.30	(0.80,1.9)
19	Case-Control Study	1992	Harlow	235	239	1.80	(1.1, 3.0)
20	Case-Control Study	1992	Rosenblatt	77	46	1.70	(.70, 3.9)
21	Case-Control Study	1992	Chen	112	224	3.90	(0.9,10.6)
22	Case-Control Study	1993	Tzonous	189	200	1.05	(.28, 3.98)
23	Case-Control Study	1995	Purdie	824	860	1.27	(1.04, 1.54)
24	Case-Control Study	1996	Shushan **	200	408	2.00	NA
25	Case-Control Study	1997	Chang	367	564	1.51	(1.13,2.02)
26	Case-Control Study	1997	Cook	313	422	1.60	(0.9, 2.9)
27	Case-Control Study	1998	Green	824	855	1.30	(1.1, 1.6)
28	Case-Control Study	1998	Godard	170	170	2.49	(0.94,6.56)
29	Case-Control Study	1999	Cramer	563	523	1.60	(1.18, 2.15)
30	Case-Control Study	1999	Wong***	499	755	1.13	(0.89, 1.43)
31	Case-Control Study	2000	Ness	767	1,367	1.50	(1.1, 2.0)
32	Case-Control Study	2004	Pike				
33	Case-Control Study	2004	Mills	256	1,122	1.74	(1.14, 2.64)
34	Case-Control Study	2008	Goodman	367	602	0.99	(.70, 1.41)
35	Case-Control Study	2008	Gates			1.41	(1.14 1.76)
36	Case-Control Study	2008	Merritt	1,576	1,509	1.34	(1.06, 1.68)
37	Case-Control Study	2009	Moorman	1,086	1,057	1.37	(1.05, 1.80)
38	Case-Control Study	2009	Wu	609	688	2.08	((1.34 3.23)
39	Case-Control Study	2011	Rosenblatt	812	1,313	1.13	(0.93,1.36)
40	Case-Control Study	2012	Lo-Cignaie	902	1,802	1.34	(1.07,1.66)
41	Case-Control Study	2012	Kurta	902	1,802	1.41	(1.16, 1.69)
42	Case-Control Study	2015	Wu	1,701	2,391	1.46	(1.27,1.69)
43	Case-Control Study	2016	Schildkraut	584	745	1.71	(1.26, 2.33)

Odds ratio, likelihood (odds) that an outcome will occur because of a particular exposure compared to the likelihood it will occur without the exposure. 95% CI, 95% confidence interval, a measure of statistical uncertainty that says with about 95% of the time that the true value is within the range of numbers. The wider the range, the higher the uncertainty. NR, not reported.

* crude unadjusted estimate

** approximate, unadjusted estimate

*** assessed perineal or thigh use, and controls all have cancer

Berge (2018) ⁶⁸

This large, comprehensive systematic review of the association between genital use of talc powder products and ovarian cancer also had well-described methods. Berge reviewed and abstracted data for 27 publications and reported an overall summary estimate of the association between talc exposure and ovarian cancer. For six of the reviewed studies, Berge included data published in a pooled data analysis, from Terry ⁶⁹ described below) that had not been previously included in the original publications. Overall, data on 15,230 women with ovarian cancer were analyzed (a number that is incorrectly reported in the paper). This is slightly higher than the number included in Penninkilampi because of the additional patients from the Terry publication. The summary estimate for risk of ovarian cancer for women who ever used genital talc was RR 1.22 (95% CI 1.13, 1.30). When stratified by histologic type, serous carcinoma was the only type with a significant association to talc use (RR 1.24, 95% CI 1.15, 1.34). There was no difference in risk when tumors were categorized as invasive versus borderline.

To assess relationships among ovarian cancer and intensity and duration of use, these measures were analyzed separately rather than as a combined measure that would give an estimate of the total number of exposures; the analyses did not demonstrate a significant dose response. Importantly, these measures were assessed only in five studies with the results on frequency of use presented as increased risk per additional day per week of talc use, which assumes a very linear association. I was not able to identify the original studies used in the review that reported the results with this level of granularity. Because of the small number of studies, the results (3% increase in risk per additional day of talc used, with high statistical uncertainty) were not surprising.

The authors also stratified the results by the study design (as did Penninkilampi) and found that the association between talc exposure and ovarian cancer was significant only for the case-control studies, although, as above, the cohort studies had the weakest definition of exposure. The primary limitation of the review is defining exposure as ever having used talc. As described above, this is a broad, vague definition that probably dilutes any estimated association, as it includes both women with trivial use and with regular use. A second limitation is that the included studies adjusted for a variety of covariates although this is unavoidable in this type of summary. The large difference in general between adjusted and crude results emphasizes the importance of adjustments when estimating particular risk.

Langseth (2008) ⁷⁰

This systematic review of the association between genital use of talc powder products and ovarian cancer included 21 publications. The overall pooled odds of cancer were OR 1.35 across all studies. Several authors of this systematic review were involved in an IARC report on talc exposure. They analyzed a subset of eight studies used in the IARC report that were considered to be the most informative for estimating ovarian cancer risk. Analysis of these more relevant, higher quality studies, produced an increased ovarian cancer risk of 30 to 60% (presumably OR 1.3–1.6) associated with talcum powder use. This subset analysis did not document a dose response or assess associations by cancer types.

Huncharek (2007) ⁷¹

Huncharek summarized the results of nine studies that reported on the association between talc used on contraceptive diaphragms and ovarian cancer. No data on perineal talc exposure were analyzed and the data are not included herein. Of note, the reported methodological details suggest a very poorly designed and conducted study. Some of the included papers do not even mention talcum powder products used with diaphragms. This systematic review is poor quality.

IARC (2006) ⁶²

Beginning in 1969 the International Agency for Research on Cancer (IARC) began a program to critically review the data on the carcinogenic risk of chemicals to humans. They subsequently expanded their reviews to include evaluation of carcinogenic risks associated with a range of exposures (including risks associated with biological and physical agents, lifestyle factors, complex mixtures of exposures, occupations, etc.) The purpose of the IARC program is to elaborate and publish detailed monographs including critical review of data, to evaluate human risks, and to indicate where uncertainty exists and where additional data are needed. They also give an overall assessment of the strength of the associations. It is worth noting that the individuals who contribute to IARC reports (the Working Group) include extremely knowledgeable and unbiased scientists who have specific content expertise and who have no apparent conflicts of interest. Invited specialists and representatives from international health agencies are brought in to supplement the scientific experts. In their evaluation, they heavily weight whether data support a conclusion of causality. They score evidenced into four categories, ranging from a) evidenced suggesting lack of carcinogenicity; b) inadequate evidence of carcinogenicity c) limited evidence of carcinogenicity and d) sufficient evidence of carcinogenicity. Category c is used when there is possibly carcinogenicity, and this category is not used lightly. An exposure meets category c if there is a positive association between observed exposure to the agent and cancer for which a causal interpretation is considered by the Working Group to be credible, but chance of bias or confounding could not be ruled out. They further categorize agents into 3 groups: Group 1, corresponding to d above (sufficient evidence), the agent is carcinogenic to humans; Group 2, which includes 2A (the agent is probably carcinogenic) and 2B: the agent is possibly carcinogenic to humans. A review focused on the risks associated with carbon black, titanium oxide and talc was published in 2006. The review included a detailed review of the individual studies examining perineal talc use as a risk factor for cancer. IARC concluded that perineal use of talc-based body powder is possibly carcinogenic to humans (Group 2B)

Huncharek (2003) ⁷²

This review of 16 studies assessed the relationship between genital exposure to talc and ovarian cancer using data for 5260 women with cancer and 6673 controls. The pooled OR for ever being exposed to perineal talc powder products was 1.33 (95% CI 1.16, 1.45). Small differences were observed in the estimated ORs by whether controls in the case-control studies were from hospital populations (OR 1.19, 95% CI 0.99, 1.4), or the general population (OR 1.38, 95% CI 1.25, 1.52). I believe these differences are small. In general, in case-control

studies, population controls are likely more relevant and valid. However, as with several of the other reviews, talcum powder exposure was assessed as any exposure rather than quantifying by intensity. No stratification by tumor subtype or invasiveness was performed.

Gross (1995) ⁷³

Gross reviewed 10 studies on the association between talc exposure and ovarian cancer using data on 1333 women with cancer and 2362 without cancer. To summarize the RR of malignant epithelial cancer types due to any exposure to talc, adjusting for ovarian cancer risk factors, the authors combined results from five studies for OR 1.29 (95% CI 1.02, 1.63). For an analysis of all cancers (borderline and invasive), they included data from seven studies for a similar OR of 1.31 (95% CI 1.08, 1.58). Notably, the authors did not provide any methodological details of how they identified, assessed, and combined studies, making the results difficult to fully interpret. As with several of the other reviews, they assessed any exposure to talc.

Harlow (1992) ⁷⁴

Harlow reviewed five previously published studies and summarized an OR, not adjusted for confounding factors, and added his own data for a crude estimated OR of 1.3 (95% CI 1.1, 1.6). Unfortunately, no methodological details were provided on how studies were identified, assessed, and combined or how exposure was defined, making the results difficult to fully interpret. Further, only the combined, estimated, non-adjusted crude OR was reported. Of note, the results of the five published studies used in the review (in contrast to the summary) are well described and of good methodological quality.

Systematic Reviews: Summary

The systematic reviews provide a remarkably consistent estimate of an approximately 30% increase in the risk of ovarian cancer associated with any talc powder products use. The studies summarized in the systematic reviews reported consistent results with little variability and closely overlapping estimates for ovarian cancer risk due to talc use. Further, the reviews suggest that the risks are greater for invasive serous cancer. I believe Penninkilampi provides a comprehensive and high quality review and his estimate is that women who regularly use talc powder products, defined as >3600 lifetime applications, have a 40% increased risk of ovarian cancer compared to women with no regular talc powder product use. The association was significant for serous cancers.

While the methodological approaches of these systematic reviews were generally valid, I believe they all shared the weakness of focusing on any talcum powder use rather than daily talcum powder use, and this motivated my own review (below).

Pooled Data

Two large studies pooled data from several studies. They are worth describing because of their larger sample size and strong methodology in comparison to the individual case-control studies.

Pooled Data 1: Terry (2013)⁶⁹

This report pooled data on ovarian cancer patients from a national research consortium and assessed the relationship between talc powder products exposure and ovarian cancer by histologic subtype and invasiveness. Data were from eight case-controlled studies and importantly included previously unpublished data. The authors tried to unify definitions across the studies, but the definitions nonetheless varied widely. The prevalence of genital powder use in the controls varied widely across participating study sites, ranging from 15%–45%, suggesting either large variations in the underlying populations or, probably more likely, variation in the definition of powder use that led to these differences.

The data were for a total of 8525 cases and 9859 controls in the primary analysis. The authors found that **genital talcum powder use was associated with an approximately 24% increased risk of epithelial ovarian cancer (OR 1.24, 95% CI 1.15, 1.33)**. When stratified by cancer type, the risk was increased for all cancers except mucinous cancer. Risks were approximately equally elevated for invasive and borderline tumors. They used a subset of patient data to determine RR of ovarian cancer for the highest talcum powder users, measured as cumulative lifetime perineal applications (defined as applications per month and months of the year). They also considered age (inclusion in the highest user group required more use at age 70 than age 40) and assessed risk of cancer among the highest users. **The odds of cancer in the highest talc exposure category was higher than for women who ever used talc (OR 1.37, 95% CI 1.19, 1.58)**. A significant dose response was seen when data on all patients were analyzed, with greater exposure leading to greater risk.

Pooled Data 2: Cramer (2016)⁷⁵

Cramer conducted several case-control studies on the relationship between genital talc powder use and ovarian cancer. He pooled data from a large number of these studies, described as reflecting study enrollment in 1992–1997, 1998–2002, and 2003–2008. This publication reports the analysis of pooled data from these separate enrollment phases and a more detailed characterization of those data. Cases were women who resided in Eastern Massachusetts and New Hampshire diagnosed with epithelial ovarian cancer between the ages of 18 and 80. Controls were women identified through random-digit dialing, driver's license lists and town resident lists. Women were interviewed in person, and details of talc use were elicited including the number of applications per month (allowing assessment of frequency of use), timing of use, and lifetime exposures. These descriptions gave far greater detail than most other reports and are thus an important contribution to the field. Further, more demographic and clinical history were obtained and described in these enrollments than for other reviewed studies. This report gave associations from pooled data for 2041 cases and 2100 controls. The larger size of the population, unified variables, and greater detail about cases and controls allowed a larger number of stratifications than other studies.

Overall, genital talc use was associated with an OR of 1.33 (95% CI 1.16, 1.52). An important observation was that risk decreased with time since last use. Thus, how often women regularly used talcum powder (daily, or weekly or monthly) was meaningful for predicting ovarian cancer risk, but not if the women had not used talcum powder for 5 or more years.

Women who reported using talcum powder daily (>30 applications per month) had an OR of 1.46 (95% CI 1.2, 1.78). Of note, among women in the ovarian cancer case group who used talcum powder, daily was the most commonly reported frequency of use. **When analysis used data on women who reported their total number of talcum powder applications, those in the highest group category (>7200 lifetime applications, the equivalent of 20 years of daily application) had an OR for ovarian cancer of 1.49 (95% CI 1.06, 2.1).**

Cramer conducted detailed analysis of factors that could influence/interact with the association between talcum powder and ovarian cancer. Some of the results are quite striking. First, a very strong interaction with race was noted. **African-American women seem to be at a particularly elevated risk of ovarian cancer following talcum powder exposure (OR 5.08, 95% CI 1.32, 19.6) compared with white women (OR 1.35, 95% CI 1.17, 1.55).** This finding calls for greater research given the higher incidence, and poorer outcomes among African American women. Asian women seem to be at reduced risk (OR 0.04, 95% CI 0.01, 0.34). **Analysis showed a strong relationship with menopausal status and use of hormone replacement therapy.** ORs were significantly increased in premenopausal women (OR 1.41, 95% CI 1.13, 1.75) and **postmenopausal women who used hormone treatment (OR 2.21, 95% CI 1.63, 3.0).** Postmenopausal women who did not use hormone therapy were not at increased risk of ovarian cancer (OR 1.0, 0.68, 1.49). **Interestingly, the risk of ovarian cancer among postmenopausal hormone-treatment users was elevated only if they used hormones before hysterectomy and tubal ligation but risk was substantial (OR 3.49, 95% CI 1.39, 8.75) if talcum powder was used before these surgeries (OR 5.85, 95% CI 2.89, 11.9) compared to talcum powder use both before and after surgery.**

These findings merit further assessment in other populations but raise the possibility that estrogen is important in ovarian carcinogenesis. The authors also stratified analyses by histologic type and found that the relationship between ovarian cancer and frequency of talcum powder use was significantly elevated for invasive and borderline serous cancer and invasive endometrioid cancer, but not for mucinous, clear cell or mucinous borderline cancer. **Among the most frequent users of talc the adjusted OR for invasive serous cancer is 1.54 (95% CI 1.15, 2.07).** This relationship was even stronger among premenopausal women (OR 1.85, 95% CI 1.21, 2.8) compared to postmenopausal women (OR 1.33, 95% CI 0.96, 1.85).

Pooled Data of Case-Control Studies: Summary

The increased risk of ovarian cancer associated with talc use was estimated at around 40% across these studies. The increased risk for serous cancer was even higher at 50%.

Case-Control Trials

A large number of case-control studies are published—too many to dedicate a paragraph to summarizing the methods of each.

21,24,36,40,74,76-99

I carefully read and abstracted data from each study. Without assessing the quality of the case-control studies, I included them in a table and sorted them by size of the reported effect

of talc on ovarian cancer risk. It's a way to get an overview of what they report – and Viewing them in this way is easy to see the general direction of the effect. All but two demonstrate a positive association ($OR > 1$) between any talc powder products use and ovarian cancer, with ORs ranging from 0.73–3.9 across studies, Table 5 .

Table 5: List of Case-Control Studies Sorted by Estimated Effect Size (Odds Ratio)

Year	First author			Odds ratio	Confidence interval
	2008	Goodman	367	602	0.99 (.70, 1.41)
1993	Tzonous	189	200	1.05	(.28, 3.98)
1989	Harlow	116	158	1.10	(0.70,2.1)
1999	Wong*	499	755	1.13	(0.89, 1.43)
2011	Rosenblatt	812	1313	1.13	(0.93,1.36)
1995	Purdie	824	860	1.27	(1.04, 1.54)
1989	Booth	235	451	1.30	(0.80,1.9)
1998	Green	824	855	1.30	(1.1, 1.6)
2008	Merritt	1576	1509	1.34	(1.06, 1.68)
2012	Lo-Cignaia	902	1802	1.34	(1.07,1.66)
2009	Moorman	1086	1057	1.37	(1.05, 1.80)
2008	Gates			1.41	(1.14, 1.76)
2012	Kurta	902	1802	1.41	(1.16, 1.69)
1988	Whittemore	188	539	1.45	(0.94, 2.22)
2015	Wu	1701	2391	1.46	(1.27,1.69)
2000	Ness	767	1367	1.50	(1.1, 2.0)
1997	Chang	367	564	1.51	(1.13,2.02)
1982	Cramer	215	215	1.58	(0.98, 2.47)
1997	Cook	313	422	1.60	(0.9, 2.9)
1999	Cramer	563	523	1.60	(1.18, 2.15)
1992	Rosenblatt	77	46	1.70	(.70, 3.9)
2016	Schildkraut	584	745	1.71	(1.26, 2.33)
2004	Mills	256	1122	1.74	(1.14, 2.64)
1992	Harlow	235	239	1.80	(1.1, 3.0)
1996	Shushan **	200	408	2.00	NA
2009	Wu	609	688	2.08	((1.34 3.23)
1998	Godard	170	170	2.49	(0.94,6.56)
1983	Hartge	135	171	2.50	(0.70, 10.0)
1992	Chen	112	224	3.90	(0.9,10.6)
2004	Pike			NA	

V. Rationale for and Explanation of the New Systematic Review

In previous systematic reviews that I have conducted, I have obtained the most meaningful and consistent results by narrowly defining the research topic of the review, including only studies that provide data on this narrow topic in a well-defined population and stratifying my analysis of the studies' results by relevant factors such as age or race/ethnicity. The benefit of this approach is more accurate, precise, and meaningful results, while the potential tradeoff is a reduction in general applicability of the results, because many studies may be excluded for inadequate data. I believe greater accuracy is more important because I want to be certain about the data I am describing. For example, when I conducted a systematic review on the use of transvaginal ultrasound as a diagnostic test for endometrial cancer, I initially stratified

the results by patient use of hormone therapy. The reviewed studies had consistent results, but only if profoundly different diagnostic criteria were applied for women who did and did not use hormone therapy. For this reason, I completed one review on hormone users and another on non-users. In this case, I had sufficient data to assess both groups.

In this review on talcum powder use, I had sufficient data to summarize results for regular users of talcum powder (as close to daily but reflecting use of talc powder products several times per week) and risks of serous cancer; I did not have sufficient data to summarize results for occasional users or risk of other cancer types. I believe the most important research question to answer in this review is whether regular exposure to talcum powder is associated with ovarian cancer. I want to point out that this does not mean that other uses (i.e. less than approximate daily use) does not cause ovarian cancer, nor that talc powder products does not cause other types types of ovarian cancer (e.g. endometrioid cancer). Thus, for the systematic review below of case-control studies on the relationship between perineal exposure to talcum powder products and ovarian cancer, I focused on whether regular use of perineal (genital) talc increases the risk of the ovarian cancer. When possible, I focused on the most common and serious type, invasive serous ovarian cancer.

VI. New Systematic Review of Literature Quantifying Association Between Regular Frequent Genital (Perineal) Talcum Powder Products Application and Ovarian Epithelial Cancer Risk with A Focus on Invasive Serous Cancer.

Literature Search

I performed a literature search to identify primary research studies (not reviews) that included patient-level data on the association between talc and ovarian cancer. The literature search was performed in the Medline, Embase, and Scopus databases using keywords “ovarian cancer,” “talc,” “perineal powder” and “genital powder.” Abstracts of resulting publications were reviewed to identify if they addressed the topic and included data. Only English-language articles were reviewed. The references of identified articles and reviews were scanned to identify additional publications. Review articles, editorials, letters to the editor were excluded.

Article Selection

Articles were included based on relevance to the question: **Does the regular (as close to approximately daily) use of genital (perineal) talcum powder increase invasive epithelial ovarian cancer?** Because daily use was the most dominant use category, when studies stratified their results into quartiles of use, or lifetime applications, I included the highest use category that had a reasonable number of data points to reflect daily use. Wherever possible, data on invasive serous cancer were abstracted separately. When I found duplicate reports on the same patient group, the largest and most detailed publication was included. This usually meant the most recent publication, but not always. An important caveat is that I could not always identify duplicative results. I included data from the Terry 2013 pooled data study because it included new data from previous studies. I also included data from the Cramer

2016 pooled analysis and earlier publications with duplicative patients were not included. But I calculated the results both including and excluding these studies.

Exclusion

Studies were not included if they reported only crude ORs unadjusted for confounding factors. A few studies were excluded because, the research methods were poorly defined, even though they reported on women who frequently used talcum powder. Studies that asked participants a single question about ever use of talcum powder, without further quantification of exposure, were not included in the summary.

Defining Talcum Powder Products Use

Regular use was defined ideally as daily or at least more than 3 uses per week. I also accepted studies that defined use as “regular” where the description made it clear that this was regular use. Studies that reported “regular use” but defined it as use of less than this frequency, were not included. Regular use was selected to differentiate occasional use (which may include one-time or infrequent use or use during only a particular time of a woman’s menstrual cycle) from sustained regular use. Studies that asked participants a single question about ever use of talc, without further quantification of exposure, were not included in the summary. For example, Purdie reported that 52–57% of women reported ever using talc without further quantification and was not included. Several studies asked about *regular use* defined as at least once a month. These studies were not included unless they further characterized women into different categories of use; if so, I included data for women in the highest use category as long as this was group was large enough to be meaningful. When studies asked about ever use but defined use and stratified results by use, I included any data that may have reflected daily use. This measure of regular use is imprecise but is more accurate and meaningful than evaluating talcum powder exposure as any use.

Stratification of Analyses: Focus on a Single Histologic Type Where Possible

My review focused on invasive serous cancer where possible, but also included all invasive cancer. The decision to focus on a single histologic cancer type was in part because ovarian cancers include a broad range of types and association of talc and ovarian cancer might differ by type. I chose serous cancers because they are most common invasive ovarian cancer type. Importantly, serous ovarian cancer is the only histologic type for which most individual research studies accumulated sufficient cases for valid statistical analysis. This cancer type also has the least uncertainty in pathological diagnosis (see Section III, Histologic Types). Further and most importantly, serous ovarian cancer is the most aggressive histologic type, so identifying causal factors is important. Finally, I focused on invasive cancer (as opposed to borderline cancer) because the risk of death from invasive serous tumors is far higher than for noninvasive types, with growing consensus that borderline tumors may not be malignant.

Type of Exposures

Studies were included if they reported on perineal exposure (rather than exposure through sanitary napkins, diaphragms, or condoms) as this is the most common exposure type and is

likely to reflect the most consistent exposure. I did not exclude studies if they reported combined use, as long as the exposure included perineal use.

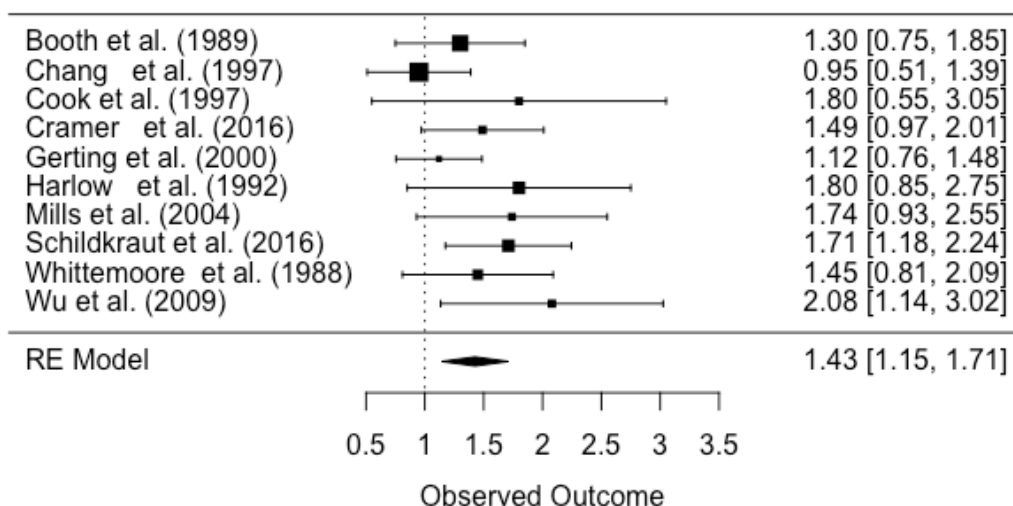
Statistical Analysis

Two individuals (Smith-Bindman and a consultant biostatistician) reviewed an abstracted data from each publication. Differences were resolved by consensus. The focus of the review was on quantifying the association between regular talcum powder products use and ovarian cancer, with a sub analysis on serous cancer and invasive cancer. Meta-analysis was performed using the metafor package in R (Version 3.5.1). The rma function was used to apply linear mixed effects models to study results and calculate summary statistics on effect size. Due to varying amounts and types of available data from each included publication, adjusted odds ratios (OR) and standard errors were used as the model inputs. Standard error (SE) was estimated using the relationship: 95% confidence interval = Effect size \pm 1.96*SE, assuming a roughly normal distribution of data and roughly symmetrical upper and lower confidence interval bounds. Incorporating adjusted ORs and SE into models in this way provides the added benefit of allowing model use of covariate-adjusted data (versus crude OR data). Weighting was done based on estimates of inverse variance. Study result heterogeneity was estimated based on maximum likelihood methods and was summarized via an I² statistic and associated p-value. The decision to include results from the cohort study by Gertig and colleagues (2000), which reported relative risk (RR), was based on the estimation that the RR value was only nominally different from the OR, a safe assumption in a study sample where less than 0.4% of the cohort developed the condition-of-interest.

Results

Overall 10 studies reported on daily talc powder products use and the risk of ovarian cancer. These studies were homogenous, and the odds of ovarian cancer associated with regular use was 1.43 (95% CI 1.15 1.71). The included studies with associated point estimates are shown in a Forrest Plot in Figure 2

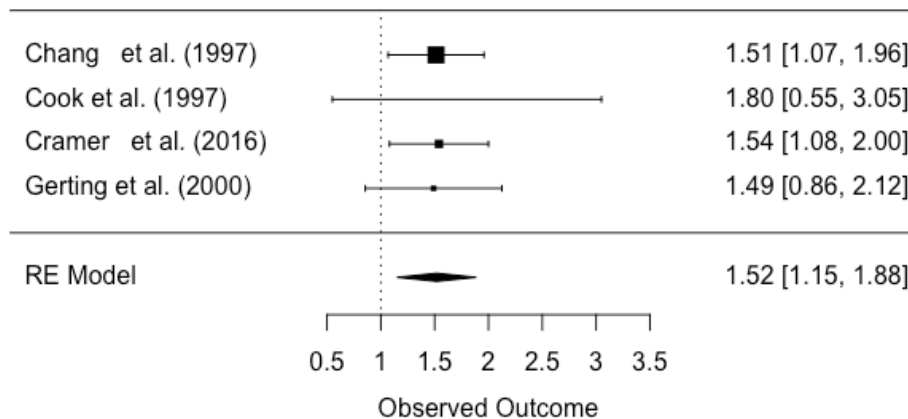
Figure 2. Forrest plot showing odds of ovarian cancer associated with regular use of talcum powder products.



The primary analysis of this excluded Terry, but the results were nearly identical if Terry was included

There were studies reported on regular talcum powder use and invasive serous cancer (or all invasive cancer if serous not reported) These studies were homogenous. The odds of invasive serous cancer associated with regular use was 1.52 (95% CI 1.15, 1.88). The results were similar when assessing the odds of all serous cancer.

Figure 3 Forrest plot showing odds of ovarian cancer associated with regular use of talcum powder products and invasive serous cancer.



New Systematic Meta-Analytic Review: Summary

The results of my systematic review of case-control studies on talcum powder use and ovarian cancer risk were consistent and indicate a **50% increase in risk of serous invasive cancer related to routine talcum powder exposure compared to no exposure**. This review had limitations including that study results were self-reported. I tried to be consistent in defining exposure, but this factor was subjectively determined by the individual studies. I tried to eliminate overlap of participant populations used in the included studies, but some patients may have contributed data to more than one study.

Overall Summary of the Epidemiology Data Describing the Association Between Talcum Powder Products and Serous Ovarian Cancer

I conclude, based on the review of the available primary studies, systematic reviews and my own quantitative review, that regular exposure to talcum powder products increases ovarian cancer risk by around 50%. The existing systematic reviews (in particular Penninkilampi and Berge) also concluded a significant increase in ovarian cancer risk following talcum powder exposure.

VII. Other Relevant Factors

Research Supporting Talcum Association with Ovarian Cancer: Transit to Ovary and Risk Reduction on Interruption

Evidence from relevant studies is clear that talcum powder particles applied to the genital region will ascend through the vagina and fallopian tubes and enter the pelvic cavity, reaching fallopian tubes and ovaries. In humans, this route has been established experimentally by labelling inert particles, applying them to the perineum just prior to planned hysterectomy, and then recovering them from the fallopian tubes following surgery. [Egli Fertil Stwriil 1961]

Further, talc particles have been found in normal and malignant ovarian tissue. Henderson found that in 10 of 13 tested epithelial ovarian cancer tumors, 75% had talc embedded in the tissue. This result confirms that talc reached to the areas with cancerous tissue, but not that it caused the cancer. Histological evaluation of ovaries removed because of ovarian cancer or benign conditions have identified both talc particles and asbestos fibers in the ovarian tissue, further supporting that particles applied to the perineum reach the ovaries.^{60,100} Heller found that in all women in a study who were having ovaries removed for benign ovarian growth had talc in their ovaries. These results confirm that talcum powder applied to the perineum may be absorbed into the vagina and migrate or be transported to the tubes and ovaries.¹⁰¹⁻¹⁰⁴ In 1967, Graham and Graham demonstrated that intraperitoneal application of asbestos in guinea pigs and rats results in overgrowth of ovarian epithelial cells comparable to the histologic changes in epithelial ovarian tumors in women. The greater frequency at which talc particles are discovered in ovarian cancerous tissue than in normal ovarian tissue further supports that these particles may be causing cancer.

Several epidemiological studies evaluated the risk of ovarian cancer associated with talcum powder products before and after women had tubal ligation or hysterectomy, which surgically removes the route by which talc reaches the ovaries. The studies strongly suggest that the increased risk of ovarian cancer associated with talcum powder products use is reduced or eliminated after tubal ligation or hysterectomy. The results support that the risk from talcum powder products is elevated when women have an open pathway from the perineum to the ovary that enables powder components to reach the ovaries via unobstructed fallopian tubes., The collective results demonstrate that talcum powder products are carcinogenic through direct transport/migration to the fallopian tubes and ovaries.

Variation in Risk when Talc Use is Discontinued

Several studies showed that the risk of ovarian cancer associated with talc powder products decreases as the time from discontinuation of powder use increases. For example, Cramer found an elevated risk of ovarian cancer with talc powder products use and the risk decreased as time since last use increased.⁷⁵

VIII. Consideration of Causality of Talc Powder Products and Ovarian Cancer : Bradford Hill Analysis

Causality is easiest to determine in studies such as randomized controlled trial, in which participants are randomized to receive or not receive a treatment, then their health is followed to see their response. However, people cannot ethically be randomized to be exposed to a potentially cancer-causing agent. Therefore, when assessing risk factors for cancer, the Bradford Hill Factors are often used. They provide a framework for assessing the weight of evidence to help decide if causality is likely, given a particular association, such as between talcum powder and ovarian cancer. The guidelines are imperfect and provide a framework as compared with an absolute set of criteria.

I address each of the Bradford Hill factors below, with my understanding of how the evidence of talcum powder products exposure supports or refutes causality. While the Bradford Hill Factors include nine aspects of association, they should not be used as a checklist for causation. Instead, they can help interpret associations and aid in inferring causality. For each factor, I have highlighted why I believe this factor is more or less important.

A) Strength of Association

It is frequently argued that the larger an apparent association, the more likely the association is to be real (causal) and important for epidemiological assessment. This would suggest that an OR of 2.0 is more likely to indicate causality and importance than an OR of 1.5. While this is often argued, I do not believe this is necessarily the case. If a risk factor increases the risk of disease by 50%, and the exposure is common, it will have a far greater impact on a number of people, in comparison to a rare exposure that has a higher associated OR. And if the association is truly one that increases risk by 50%, then this is the magnitude of the association that will be detected. It is not intuitive that if an exposure increases a risk by 50%, this difference is not discoverable compared with an exposure that increases risk by 100%. A larger association between exposure and disease may be easier to identify, but I do not believe it is more likely to indicate causality or importance.

As an example, Table 6 shows an overview of the relationship between bladder cancer and two of its known risk factors; occupational industrial chemicals and smoking. Several industrial chemicals such as 2-naphthylamine are strongly associated with bladder cancer risk. In 1954, Case et al. reported a 200-fold increased bladder cancer risk for workers exposed to 2-naphthylamine. In cohort studies of rubber industry workers, elevated standardized mortality ratios (SMRs) as high as 253 (95% CI 93, 551) were reported. Use of some of these chemicals are now prohibited in Europe and their use is regulated in the United States because they cause cancer.(OSHA, 2011).

Cigarette smoking is also a known bladder cancer risk factor. However, the RR for smoking and bladder cancer is around 3, and therefore about 100 times lower than the RR for exposure to industrial chemicals. Yet bladder cancer is the second most common cancer attributed to smoking in the United States. It impacts a very large number of individuals. Of the 70,000 cases of bladder cancer diagnosed each year, as many as 60% are estimated as attributable to smoking.

Using the RR magnitude to quantify the “importance” of these two risk factors, industrial chemicals and smoking, would be misleading. Smoking will result in far more cancers than industrial chemicals, even though the RR is much lower. In the crude data in Table 6, of the approximately 70,000 bladder cancers diagnosed annually in the United States, 50,000 are thought to result from cigarettes while fewer than 1000 result from occupational exposures. A 50% reduction in smoking exposure will save 25,000 men from getting bladder cancer. Reducing industrial chemical exposures will saving around 500 men from getting bladder cancer. Thus, any impact on reducing known exposures for bladder cancer has the potential to be around 50 times more impactful if directed at smoking.

Table 6. An example showing the number of individuals who might be impacted through exposure to an occupational chemical that leads to bladder cancer as opposed to smoking.

	Occupational Exposure	
	2-naphthylamine	Smoking
Estimated odds ratio associated with exposure	200	3
Number of individuals exposed annually	10,000	50,000,000
Bladder cancers due to exposure annually	1000	50,000
Impact on number of cancers diagnosed annual if exposure reduced by 50%	500	25,000

The bladder cancer example highlights that a factor that increases risk by 50% will have an enormous impact on population mortality if the exposure is common or if the cancer is particularly lethal. This is certainly the case for talcum powder products, which are used by as many as half of all women in the U.S. Women’s use of talcum powder products is so widespread that even a relatively modest increase in risk would pose a sizeable health risk to the population. Further, a 50% risk increase is particularly important for ovarian cancer, which has a high mortality rate, with rare early detection.

Defining a “strong” association is critical for assessing potentially causal relationships. A current concept in epidemiology is that considerations about whether a factor causes a disease should weigh statistical validity and significance and the multiple factors that influence the disease. Thus, assessing *strength of association* when inferring causality requires examining underlying research and analytic methods, comparing the weight of evidence in the literature, and considering other contextual factors. The data supporting the causality of talcum powder products exposure for ovarian cancer is extremely strong.

Using the existing evidence, I reviewed and assembled for this report, I estimated how many ovarian cancers that occur each year in the United States are likely to be caused by exposure to talcum powder products in comparison to other risk factors for ovarian cancer, Table 7. This is a relatively simple analysis, but nonetheless is informative. The total number of ovarian cancers that are estimated to occur in the US annually is 22,240, and these will occur among

the 50.8 percent of the U.S. population of 311 million who are women. Of these ovarian cancer cases, approximately half (11,120) will reflect invasive serous carcinoma. For the purpose of this simple analysis, I have assumed that the elevation in ovarian cancer risk associated with talcum powder product exposures occurs only with invasive serous carcinoma. This is not true, but the data are the most certain for these cancer and this is a conservative assumption (meaning the true number of cancer and proportion of cancers caused by talcum powder product users will be even higher than my calculation). A proportion of ovarian cancers will occur among women who regularly use talcum powder products, and the remainder will occur in women who do not regularly use talcum powder products. If we estimate that women who use talcum powder products regularly have a 50% elevated risk of invasive serious cancer and we estimate the number of women who are exposed to daily talcum powder products is between 10% and 30% (this proportion is fewer than ever users of talcum powder products), then between 1,589 and 4,351 women will be diagnosed each year with invasive serous cancer caused by the exposures, reflecting between 14% and 39% of all invasive serous cancers and reflecting between 7% - 20% of all ovarian cancer diagnosed each year. This is a tremendous risk. This is a very large number of cancers to be caused by a product that provides no medical benefit. This Bradford Hill Factor of the Strength of the association is important and is met.

Table 7 An estimate of the number of ovarian cancers and invasive serous cancers caused by regular use of perineal talc powder products.

Proportion of women who regularly use Talcum powder products	Annual Invasive Serous Cancer in Women Exposed to Talcum Powder Products	Annual Invasive Serous Cancer in Women Not Exposed to Talcum Powder Products	% Invasive Serous Cancer in Women Exposed to Talcum Powder Products	% of all ovarian Cancer in Women Exposed to Talcum Powder Products
10%	1,589	9,531	0.14	0.07
20%	3,033	8,087	0.27	0.14
30%	4,351	6,769	0.39	0.20

B) Consistency of Associations in Different Populations and Studies

Another consideration for association and causality is consistency of the data. The data on the association between genital talc and ovarian cancer are highly consistent. The relative stability in the estimated increase in the risk of ovarian cancer associated with talc powder products use (50% increase for regular users of talcum powder and serous cancers; around 40% increase for all epithelial ovarian cancer and regular users of talcum powder products), as assessed across time and in diverse populations with diverse study designs, strongly argues that the causal association is real and satisfies the Bradford Hill guideline for consistency of associations across populations and studies.

C) Specificity Between Cause and Effect

The Bradford Hill factors suggest that associations are more likely to be causal when an exposure causes only one disease. While some examples of highly specific exposures and outcomes exist, many exposures and health concerns involve complex chemical mixtures and low-dose environmental and occupational exposures complicated by a variety of personal risk factors. A recent review stated, "The original criterion of *specificity* is widely considered weak or irrelevant from an epidemiologic standpoint."¹⁰⁵ Asbestos, for example, is associated with a range of cancers and various exposures. Regardless of doubts about the meaningfulness of this factor, talcum powder products are primarily associated with ovarian cancer and thus fulfills the specificity consideration, although this consideration is not one of the most important considerations for causality in my expert opinion.

D) Temporality

An exposure must come before an outcome for the exposure to be causal. Bradford Hill explained that for an exposure-disease relationship to be causal, exposure must precede the onset of disease. While this is self-evident, in epidemiological studies, reverse causality, in which behavior related to a health issue is influenced by knowledge or events about the issue, is always a concern. For example, women who undergo ovarian cancer treatment may begin using talcum powder products during their pre- and post-operative period because of symptoms or side effects perceived to be alleviated by talcum powder products use. Assessing talcum powder use without specifying the time of use might lead to women with ovarian cancer being more likely to report talcum powder products use. In this example, talcum powder may not have caused the cancer; rather, use of talcum powder products was caused by the cancer (and treatments). The importance of this issue led to Bradford Hill's consideration of temporality when assessing causality.

In essentially all of the case-control studies that assessed use of talcum powder products, women were specifically asked to report talc powder products only during past, not current periods; thus, the studies explicitly assessed exposure to talcum before cancer. Typically, questions were phrased "Did you ever use talc, but not in the last year before cancer diagnosis?" to exclude the year prior to diagnosis. This issue is not relevant for the included cohort studies, as women were surveyed about their exposures prior to cancer ascertainment. Thus, the temporality consideration is important for my consideration and is satisfied.

E) Dose Response

In general, when risks are proportional to exposure (e.g., doubling exposure doubles risk) this dose-response evidence is considered to support causality. Many of the reviewed studies did not collect sufficient data to carefully quantify the dose response, and many limited their comparisons to an ever/never comparison. This is in part what motivated me to complete my separate quantitative review to at least be able to dis-entangle ever into regular versus not regular use. The reviewed studies that did provide data that could be used to assess the

potential for dose response had mixed results in quantifying dose response. While most studies showed evidence of a dose response, others did not. For example, Schildkraut showed that >20 years of any genital powder use (OR 1.51, 95% CI 1.11, 2.06) showed a stronger association with ovarian cancer than <20 years of use (OR 1.33, 95% CI 0.95, 1.86).⁹⁹ Terry and Harlow showed significant dose responses, where ORs increased as exposures increased.^{69,74} The adjusted ORs increased from 1.3, to 1.5 to 1.8 with <1000, 1000–10,000, and >10,000 lifetime applications. Overall, any exposure to talcum powder resulted in an OR of 1.5; direct perineal application had an OR of 1.7 (95% CI 1.1, 2.7), daily exposure had an OR of 1.8 (95% CI 1.1, 3.0) and women with an intact genital tract who were estimated to have had more than 10,000 applications during ovulating years had the highest risk (OR 2.8 95% CI 1.4, 5.4). This exposure was found in 14% of women with ovarian cancer. Penninkilampi⁶⁷, the most comprehensive of the systematic reviews, also showed a dose response where women with more than 3600 lifetime applications had slightly higher risks as did women who reported long-term (>10 years) talc use. In contrast, Whittemore⁷⁷ showed no dose response, and Booth⁷⁸ demonstrated the reverse—the higher the dose, the lower the risks. The data from reviewed studies were too diverse to summarize a dose-response relationship. The measures of exposure frequency and duration varied, and the studies used different thresholds for quantifying exposures. Further, the measures to quantify dose tended to be crude, making the response even more difficult to establish.

In summary, most but not all studies of talcum powder products and ovarian cancer show a dose response, but the results are inconsistent, and more importantly, are not considered or assessed in most of the published studies. A dose-response relationship is not required for causality and in large part because data were not consistently available, this factor does not weight heavily in my consideration. Further, this factor did not weight heavily in my considerations in that not all exposures will have a dose response, and some will indeed have a threshold effect. This is important here because asbestos is believed to exhibit a threshold, rather than a linear, dose-response.

F) Biologic Plausibility: Factors Linking Talc and Ovarian Cancer

The epidemiological evidence suggests a strong and positive association between exposure to talcum powder products and invasive ovarian cancer. However, epidemiological evidence alone does not provide a mechanism or pathophysiological process that accounts for the increased risk. Nor does the epidemiological evidence confirm the specific component or ingredient in talc powder products that is responsible for carcinogenesis. Nonetheless, the data are persuasive that particles contained in talcum powder reach the tubes and ovaries, inflammation initiate a causal pathway, and that several components of talc powder products including asbestos, asbestiform fibers in talc, and heavy metals can contribute to the carcinogenicity of the products. This was a strong factor in my consideration of the evidence because there is extremely strong evidence that the components of talc powder products are known to be highly carcinogenic in other settings.

G) Coherence and Consistency with Understood Biology

The guideline of coherence is considered similar to biological plausibility. For both, the cause-and-effect explanation should be consistent with all knowledge available. For talcum powder and ovarian cancer, this consideration is easily satisfied.

H) Experimental Evidence

The evidence in humans of the impact of talcum powder products exposure and ovarian cancer development is based on a large number of observational studies. Direct experimental evidence in the form of randomized controlled trials in humans is simply not possible to generate, for ethical reasons. The experimental evidence in humans that talc particles can migrate to the ovary and be incorporated into ovarian tissue is relevant to developing a causal model but does not directly prove that that exposure causes cancer. There is also human data relating to the inflammatory nature of ovarian cancer. There is compelling in vitro research delineating the inflammatory mechanism by which talcum powder causes cancer. Animal studies showing inflammatory tissue effects and tumor formation with talcum powder exposure are also supportive.

I) Analogy

Bradford Hill implied that when evidence is strong of a causal relationship between a risk factor and disease, researchers should be more accepting of weaker evidence that a similar risk factor may cause a similar disease. Thus, analogy has been interpreted to mean that when one causal agent is known, the standards of evidence are lowered for a second causal agent that is similar. The strong evidence for the association between asbestos and lung cancer, and the chemical similarity between these minerals, as well as their fibrous nature, supports the analogy consideration and causal inference.

Summary: Consideration of Causality of Talc Powder Products and Ovarian Cancer using Bradford Hill

In consideration of Bradford Hill, the clear strength of the association (A), remarkable consistency in the published literature across a large number of populations and research studies (B), temporality (D) considered in all of the published studies, and perhaps most importantly, biological plausibility (F) were the criteria that I considered of paramount importance when assessing the causality of exposures of talc powder products and epithelial ovarian cancer

IX. Conclusion

In conclusion, substantial evidence supports a strong, positive and causal association between ovarian cancer and genital exposure to talcum powder products. Regular exposure to talcum powder products causes ovarian cancer in some women. This opinion is based on my extensive review of the medical and scientific literature, my own independent meta-analysis of the data, and my experience and expertise in the areas of epidemiology and women's health, including ovarian cancer.

All opinions are made to a reasonable degree of medical and scientific certainty. I reserve the right to amend or supplement this report as new information becomes available.

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102. Sjosten AC, Ellis H, Edelstam GA. Retrograde migration of glove powder in the human female genital tract. *Human reproduction (Oxford, England)*. 2004;19(4):991-995.
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Exhibit A

CURRICULUM VITAE
REBECCA SMITH-BINDMAN, MD

Title Professor, Radiology and Biomedical Imaging, Epidemiology and Biostatistics,
Obstetrics, Gynecology and Reproductive Sciences, Phillip R. Lee Institute for Health Policy
Director, Radiology Outcomes Research Lab, University of California San Francisco

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350 Parnassus Ave, Suite 307
San Francisco, CA 94117
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EDUCATION

1980 - 1985	Princeton University	BSE	Engineering / Architecture
1985 - 1986	Columbia University		Post Bacc Pre-Med
1987 - 1991	University of California, San Francisco	MD	Medicine
1991 - 1992	University of California, San Francisco	Intern	Pathology
1992 - 1996	University of California, San Francisco	Resident	Radiology
1996 - 1997	University of California, San Francisco	Clinical Instructor	Radiology, Ultrasound
1996 - 1998	University of California, San Francisco	Fellow	Epidemiology & Biostatistics

LICENSES, CERTIFICATION

1992	California Medical License # G76462
1993	California X-ray Supervisor and Operator License RHL 143658
1996	Board Certification, American Board of Radiology

PRINCIPAL POSITIONS HELD

1998 - 2003	UCSF, Radiology and Biomedical Imaging, Epidemiology and Biostatistics, Obstetrics, Gynecology and Reproductive Sciences	Assistant Professor
2003 - 2009	UCSF, Radiology and Biomedical Imaging, Epidemiology and Biostatistics, Obstetrics, Gynecology and Reproductive Sciences	Associate Professor
2009 - current	UCSF, Radiology and Biomedical Imaging, Epidemiology and Biostatistics, Obstetrics, Gynecology and Reproductive Sciences	Professor
2014 - current	UCSF, Phillip R. Lee Institute for Health Policy Studies	Member
2000 - current	UCSF, Radiology Outcomes Research Lab	Director

OTHER POSITIONS HELD CONCURRENTLY

1999 - 2000	St Bartholomew's and The Royal London School of Medicine	Research Fellow
2009 - 2010	NIH, National Cancer Institute, Radiation Epidemiology Branch	Research Scientist

HONORS AND AWARDS

1985	Cum laude, Princeton University
1985	Senior Thesis Prize, Princeton University
1991	Student Summer Research Fellowship, Institute for Health Policy Studies, UCSF
1999, 2000	Nycomed Amersham Fellow, Radiologic Society of North America
2007	Nomination, Clinical Research Mentor of the Year, Bay Area Symposium on Clinical Research
2010	Nomination, CTSI Consultant of the Year, Impact Award
2010	Scientific Paper of the Year, Minnies, Auntminnie.com
2010	Finalist, Most Influential Radiology Researcher, Minnies, Auntminnie.com
2011	Leader in Imaging, Auntminnie.com
2012	Finalist, Scientific Paper of the Year, Auntminnie.com, Minnies
2012	Semifinalist, Scientific Paper of the Year, Auntminnie.com, Minnies
2012	Winner, UCSF Center for Health Care Value, Medical Center Initiative, Innovation Award
2013	Finalist, Scientific Paper of the Year, Auntminnie.com, Minnies
2013	Runner-up, Scientific Paper of the Year, Auntminnie.com, Minnies
2013	Paper honored as 1 of the top 10 publications Funded by NCI's Epidemiology and Genomics Research Program
2014	Invited Editor, J of the American College of Radiology, March 2014, Radiation Dose Optimization
2014	Among Philip R. Lee Institute for Health Policy Studies faculty videos on UCTV, "Is Medical Imaging Harmful to Health: Opportunities to Influence Health Policy", most popular, N = 409,937
2015	Academy of Radiology Research, Distinguished Investigator Award
2015	Election to Fellowship, Society of Radiologists in Ultrasound

KEYWORDS AND AREAS OF INTEREST

Health Services Research, Outcomes Research, Disparities Research, Women's Imaging, Comparative Effectiveness Research, Quality Improvement, Dissemination and Implementation Sciences, Evidenced Based Radiology, Assessment of Population Impact of Screening Tests, Radiation Associated with Medical Imaging, Radiation as an Environmental Cause of Cancer, Management of Incidental Findings on Diagnostic Testing

OVERVIEW

Narrative

Dr. Smith-Bindman is a clinical researcher with expertise in health services research, epidemiology, outcomes research, comparative effectiveness research, and dissemination and implementation sciences focused on diagnostic imaging. Her research has focused on evaluating the quality, utilization, accuracy, predictive values and impact of diagnostic testing on patient health, and has quantified both the risks and benefits of medical imaging when used in different contexts and by different populations. One area of focus has been on evaluating racial and ethnic differences in access and utilization of screening mammography and how that contributes to higher breast cancer mortality among African American women, and on factors that influence the quality and access to screening among vulnerable populations (see references 33, 34, 37, 43, 46, 48, 61, 67 at the end of CV). A separate area of focus has been on quantified the variation in radiation dose associated with medical imaging across patients and institutions, and quantified the impact of radiation, particularly from computed tomography, as an environmental carcinogen. (see references 53, 58, 60, 62, 65, 68, 69, 72, 76, 78, 79., 81, 87, 89, 91, 97, 102, 107.) Separate from her research activities, she has been actively involved in translating evidence into changes in practice and policy. She has *informed policy leaders, practitioners and the public about* the safety concerns surrounding the use of radiation in imaging by describing the issue in main stream media, testifying before the US Congress, and by advising the FDA, The Joint Commission, the International Atomic Energy Agency, the International Council on Radiation Protection and leading professional societies. She has also written quality measures focused on radiation safety, and her work has resulted in organizations which monitor health care quality to adopt measures of diagnostic imaging safety.

Significant Publications

1. **Smith-Bindman** et al. Ultrasound vs Computed Tomography for Suspected Nephrolithiasis NEJM. 2014; 371:1100-10
2. Miglioretti DL, Johnson E, William SA, Grenlee RT, Weinmann S, Solberg LI, Feigelson HS, Roblin D, Flynn MJ, Vanneman N, **Smith-Bindman R**. The use of computed tomography in pediatrics and the associated radiation exposure and estimated cancer risk. JAMA Pediatr. 2013 167 (88): 700-7
3. **Smith-Bindman R**, et al. Risk of Thyroid Cancer based on Thyroid Ultrasound Imaging Characteristic: Result of A Population Based-Study. JAMA Internal Medicine. 2013 173(19):1788-96
4. **Smith-Bindman R**. Appendix F. Ionizing Radiation Exposure to the US Population, with a Focus on Radiation from Medical Imaging, included in Breast and the Environment: A Life Course Approach. The Institute of Medicine. March 20 2012
5. **Smith-Bindman R et al**. Radiation dose associated with common computed tomography examinations and the associated lifetime attributable risk of cancer. JAMA Internal Medicine 2009;169(22):2078-86
6. Curtis E, Quale C, Haggstrom D, **Smith-Bindman R**. Racial and Ethnic Differences in Breast Cancer Survival: How Much Is Explained By Screening, Tumor Severity, Biology, Treatment, and Co-morbidities. Cancer 2008 112(1):171
7. Goldman L, Haneuse S, Miglioretti D, Kerlikoswke K, Buist D, Yankaskas B, **Smith-Bindman R**, An assessment of the quality of mammography care at facilities treating medically vulnerable populations Medical Care 2008 46(7):701-8.
8. **Smith-Bindman et al**. Does Utilization of Screening Mammography Explain Racial and Ethnic Differences in Breast Cancer? Ann Intern Med. 2006; 144(8):541-53
9. Haggstrom DA, Quale C, **Smith-Bindman R**. Differences in the Quality of Breast Cancer Care Among Vulnerable Populations. Cancer. 2005 Dec 1;104(11):2347-58.
10. **Smith-Bindman, R**, et al Endovaginal ultrasound to evaluate endometrial abnormalities. JAMA 1999;281:1693-4

PROFESSIONAL ACTIVITIES

CLINICAL

Attending physician, Ultrasound Section, Department of Radiology and Biomedical Imaging, UCSF, 25%. Includes supervised instruction of residents and fellows. My teaching focuses on how to use evidence to help inform interpretation of clinical examinations.

PROFESSIONAL ORGANIZATIONS

Memberships

1997 - 2018	Society of Radiologists in Ultrasound (SRU)
1997 - 2018	Radiology Alliance for Health Services Research in Radiology (RAHSR)
2013 - 2018	American College of Radiology (ACR)
2014 - 2018	American Roentgen Ray Society (ARRS)
2014 - 2018	Association of University Radiologists (AUR)

Service to Professional Organizations (selected)

2010 - 2011	American Board of Medical Specialties, American Board of Radiology, American College of Radiology, and Physician Consortium for Performance Improvements. Patient Radiation Dose Work Group
2011 - 2012	Institute of Medicine Committee on Breast Cancer and the Environment, commissioned report "Temporal Changes in Ionizing Radiation and Estimate of Contributions to Breast Cancer," contributing author
2012	Centers for Disease Control and Prevention, Cancer Prevention Work Group
2012 - 2014	The Joint Commission, Diagnostic Ionizing Radiation and Magnetic Resonance work group focused on issues of safety and guideline development
2012 - Present	International Council on Radiation Protection (ICRP) Task Group #79 on Defining Effective Dose Use in Medicine
2014	International Atomic Energy Agency (IAEA) United Nations General Assembly and Security Council. Special Committee Considering Population Impact of Low Dose Radiation
2015	Council of Distinguished Investigators of the Academy of Radiology Research

Service to Professional Publications (selected)

2000 - 2018	Journal of the American Medical Association (JAMA)
2000 - 2018	JAMA Internal Medicine
2000 - 2018	New England Journal of Medicine (NEJM)
2000 - 2018	Radiology
2000 - 2018	American Journal of Radiology
2000 - 2011	Journal of the National Cancer Institute
2000 - 2011	Health Affairs

2000 - 2015	Health Services Research
2000 - 2010	American Journal of Obstetrics & Gynecology
2000 - 2010	American Journal of Public Health
2000 - 2010	Annals of Internal Medicine
2000 - 2010	Journal of Medical Screening
2000 - 2010	Journal of Women's Health
2000 - 2010	Medical Care
2000 - 2010	Medical Decision Making
2000 - 2010	Obstetrics and Gynecology
2000 - 2010	Ultrasound in Obstetrics & Gynecology

INVITED PRESENTATIONS

International

2001	US - UK Cancer Learning Network, Deprivation and Cancer, <i>London, United Kingdom</i>
2001	British Society of Human Genetics, Prenatal Screening for Down syndrome in England and Wales and Birth Outcomes, <i>London, United Kingdom</i>
2002	Global Summit on Mammographic Screening, Europe Institute of Oncology, U.S.-U.K. Comparison of Screening Mammography, <i>Milan, Italy</i>
2005	University of Copenhagen, Does Practice Make Perfect; Association Between Volume and Accuracy of Mammography, <i>Copenhagen, Denmark</i>
2006	International Society for Prenatal Diagnosis, Prenatal Screening for Down syndrome in The Second Trimester of Pregnancy, <i>Kyoto, Japan</i>
2009	Canadian Breast Cancer Foundation, Forum on the Earlier Detection and Diagnosis of Breast Cancer, <i>Toronto, Canada</i>
2010	Nation Cancer Research Institute (NCRI), Risk of Cancer from Computed Tomography Examinations, <i>Liverpool, United Kingdom</i>
2013	Bach Mai University Hospital, Radiation for Medical Imaging: A Hidden Epidemic, <i>Hanoi, Vietnam</i>
2014	International Atomic Energy Agency (IAEA), Health Effects of Exposure to Low Dose Ionizing Radiation Associated with Medical Imaging, <i>Vienna, Austria</i>
2014	Korea College of Radiology, Tracking and Monitoring Radiation Dose and Its Impact Across the University of California Medical Centers and CT Radiation Doses Are Not What You Think: Why It's Important to Monitor and Track Dose Seoul, Republic of Korea
2016	International Atomic Energy Agency (IAEA), Exposure to low dose ionizing radiation from medical imaging and the health effects from these exposures. International Atomic Energy Agency. Technical Meeting on Science, Technology and Society Perspectives on Nuclear Science, Radiation and Human Health: The View from Asia, Singapore University
2016	University of North Carolina School of Medicine, Chapill Hill, NC, Radiology Department Grand Rounds , Diagnostic Imaging: Increasing Effectiveness and Safety Radiation From Medical Imaging,

- 2016 Singapore General Hospital, Singapore. Radiology Grand Rounds. Visualizing Patients and Their Dose to Improve Health Care Quality,
- 2016 St Luke's International Hospital, Tokyo, Japan. Hospital-wide grand rounds, Radiation from Medical imaging: A Hidden Epidemic.
- 2017 Childhood Leukemia International Consortium, Annual Meeting, Minneapolis, Minnesota, Estimating Radiation Exposure from Imaging Procedures
- 2017 Charity Hospital, Berlin, Germany. Radiology Grand Rounds, Radiation from Medical Imaging: A Hidden Epidemic
- 2017 Charity Hospital, Berlin, Germany, Imaging for Suspected Nephrolithiasis: Results from the Randomized Controlled Trial
- 2017 University Hospital, Basel, Switzerland, Radiology Grand Rounds. A Dose of Reality: The Need for Active CT Dose Management
- 2017 Center for Diagnostic Imaging Quality Institute Council of Medical Directors, Scottsdale, AZ Keynote: Radiation from Medical Imaging
- 2017 The Leap Frog Group Pediatric Computed Tomography Radiation Dose
- 2017 PCORI Advisory Panel on Communication and Dissemination Research Presentation UCSF CT Radiation Dose Registry to Ensure a Patient-Centered Approach for Imaging
- 2017 American Urological Association (AUA) Quality Improvement Summit, Baltimore Maryland Keynote Address. Imaging Wisely: Improving the Value of Medical Imaging
- 2018 Jakarta Radiology Society, Jakarta Indonesia. Dose Optimization Implementation to achieve better radiology service in Hospital Keynote Addresses: Radiation from Medical Imaging: A Hidden Epidemic and Optimizing Radiation Doses for CT
- 2018 Westmead Hospital Sydney Australia. Radiology Grand Rounds. Radiation from Medical Imaging: A Hidden Epidemic
- 2018 Westmead Childrens Hospital, Sydney Australia. Optiizing Radiation Doses For Pediatric CT
- National
- 2000 American College of Medical Genetics
- 2000 Society of Radiologists in Ultrasound
- 2000 Society for Health Services Research in Radiology
- 2001 Society of Radiologists in Ultrasound Annual Meeting

2001	Society for Health Services Research in Radiology
2002	Society of Radiologists in Ultrasound
2003	Breast Cancer Surveillance Consortium
2003	Society of Radiologists in Ultrasound
2003	Centers for Disease Control and Prevention
2003	RSNA 88th Scientific Assembly and Annual Meeting
2004	Institute of Medicine (IOM): Saving Women's Lives
2004	Breast Cancer Surveillance Consortium
2005	Improving Mammographic Quality Standards Institute of Medicine (IOM)
2006	Beth Israel Deaconess Medical Center, Grand Rounds
2006	National Institute Child Health and Human Development
2007	National Cancer Institute, National Institute of Health (x2)
2008	Mount Sinai Urban Health Institute; Metro Chicago Breast Cancer Taskforce, Partnerships in Translation: Advancing Research and Clinical Care
2008	University of Washington, Seattle, Washington, Grand Rounds, and Visiting Professor,
2008	HMO Research Network Conference (4 th annual), Danville, Pennsylvania
2009	Society of Radiologists in Ultrasound, National Conference on Management of Ovarian Cysts
2009	Canadian Forum for the Earlier Detection and Diagnosis of Breast Cancer
2010	Center for Disease Control & Prevention, Annual Cancer Registry Meeting, Atlanta, Georgia
2010	HMO Research Network conference, Emerging Frontier in Healthcare, Research Delivery, Austin, Texas
2010	National Council on Radiation Protection (NCRP), Communication of Radiation Benefits and Risks in Decision Making
2010	National Cancer Institute, Board of Scientific Advisors, Bethesda, Maryland
2010	American Statistical Association Conference on Radiation Health, Annapolis, Maryland
2010	Breast Cancer Surveillance Consortium Annual Meeting, Washington, D.C.
2010	Kaiser Permanente: National Radiology Leadership Group, held at the RSNA, Chicago, IL
2011	Cleveland Clinic, Health Care Quality Innovation, Cleveland, Ohio
2011	Auntminnie.com, Live WebEx Conference RADEXPO 2011
2011	University of New Mexico, Visiting Professor, External Reviewer, Resident Research Day
2011	Oregon Health Sciences University, Department of Emergency Medicine, Grand Rounds
2012	Society for Imaging Informatics for Medicine (SIIM), San Francisco, CA
2012	Brown University, Grand Rounds, Emergency Medicine, RI Hospital, Providence, RI
2012	Society for Imaging Informatics in Medicine (SIIM), Los Angeles, CA

2012 PharmMed OUT, Georgetown University, Washington, DC

2012 Agency for Healthcare Research and Quality, Rockville, MD

2012 Radiology Society of North America, expert witness in full day mock trial focused on radiation safety and whether radiologists need to communicate risks to patients, Chicago, IL

2012 University of Pennsylvania, Grand Rounds, Emergency Medicine, Philadelphia, PA

2013 Radiology Society of North America (RSNA), Controversies Session, CT Radiation and Risk: How Certain Are We of the Uncertainty? Chicago, IL

2013 American Cancer Society, Doc Talk Lecture Series

2013 Association of University Radiologists (AUR), Comparative Effectiveness and Patient-centered Outcomes Research, Los Angeles, CA

2014 Cancer.net Podcast, "CT Scans and Cancer Risk", Available Online at <http://www.cancer.net/blog/2014-10/ct-scans-and-cancer-risk>

2014 Oregon Chapter, American College of Emergency Physicians, Portland, Oregon

2015 Women in Government Foundation (non-profit, non-partisan organization of all U.S. female state legislators) Diagnostic Imaging. Increasing Its Effectiveness and Safety, at 16th Annual Southern & Eastern Regional Conference, Charleston S Carolina

2016 Lindeberger Cancer Center, University of North Carolina, Chappil Hill NC, Radiation From Medical Imaging: A Hidden Epidemic

2017 American Urological Association (AUA) Quality Improvement Summit, Baltimore Maryland Keynote Address. Imaging Wisely: Improving the Value of Medical Imaging

Regional Presentations (selected)

2000 Kaiser Permanente Department of Genetics, Oakland CA

2001 San Francisco State University, SF CA

2001 UCSF, San Francisco General Hospital, Department of Medicine, Grand Rounds

2001 American College of Obstetrics and Gynecology

2002 UCSF Breast Oncology Program Comprehensive Cancer Center Grand Rounds

2003 UCSF Obstetrics and Gynecology Grand Rounds, SF CA

2004 UCSF Multi-Department Symposium. Racial Disparity and Breast Cancer, SF CA

2004 UCSF Quality of Breast Cancer Care Symposium, SF CA

2005 Sisters Network, San Francisco (African American Advocacy Organization)

2005 Stanford University, Department of Health Research and Policy, Grand Rounds, Palo Alto CA

2006 UCSF, Lunch and Learn: San Francisco Community Outreach, SF CA

2006 Bay Area Health Care and Quality Outcomes, San Francisco, CA

2007 California Breast Cancer Research Symposium, Los Angeles, CA

2010 Bay Area Clinical Research Symposium, Plenary Speaker, San Francisco CA

2011	UCSF Department of Medicine Grand Rounds, San Francisco, CA
2011	San Francisco General Hospital Department of Medicine, Grand Rounds, San Francisco, CA
2011	UCSF, Department of Urology Grand Rounds, San Francisco, CA
2011	UCSF Department of Radiology Grand Rounds, San Francisco, CA
2011	Eden Hospital, Department of Medicine Grand Rounds, Alameda, CA
2011	Stanford Hospital, Department of Medicine, Grand Rounds, Palo Alto, CA
2011	Kaiser Permanente Medical Center, Multi-departmental Grand Rounds, San Francisco, CA
2011	UCSF Institute for Health Policy Studies, San Francisco, CA.
2012	Kaiser Permanente Medical Center, Grand Rounds, San Francisco, CA
2012	Kaiser Permanente Medical Center, Grand Rounds, Oakland, CA
2012	Massachusetts General Hospital, Department of Emergency Medicine, Grand Rounds Boston,
2012	Beth Israel Hospital, Department of Emergency Medicine Grand Rounds, Boston, MA
2012	Univ. of California Office of the President, Quality Improvement and Technology, Oakland, CA
2012	UCSF, Department of Radiation Oncology, Grand Rounds,
2012	Southern California Kaiser Radiology Chiefs Grand Rounds,
2014	UCSF, Endocrine Grand Rounds, San Francisco, CA
2015	California Society of Radiology Technologists, Annual Meeting, San Francisco, CA Keynote Address. Radiation from CT: A Hidden Epidemic. Strategies to minimize doses: What technologists can do?
2016	Society of Radiology in Ultrasound, Annual Meeting, Baltimore Maryland. Risk of Thyroid Cancer Based on Thyroid Ultrasound Imaging Characteristics
2016	UCSF, Breast Oncology Program, Radiation from Medical Imaging: A Hidden Epidemic and Approaches for Improving.
2016	UCSF Mini-Medical School Radiation Safety and Medical Imaging
2017	University of California Davis, Radiology Grand Rounds, Radiation from Medical Imaging; A Hidden Epidemic
2017	UCSF: Stand Up for Science: Panel Discussant

GOVERNMENT AND OTHER PROFESSIONAL SERVICE (selected)

2002 - 2003	CDC, National Breast and Cervical Cancer Early Detection Program, Planning Committee
2002 - 2005	Cochrane Collaboration Screening and Diagnostic Tests, Methods Working Group
2003 - 2003	Radiology National Boards, Examination Question Writer
2003 - 2010	National Cancer Institute, Physician Data Query (PDQ)

2004 - 2005	CDC, National Breast and Cervical Cancer Early Detection Program, Panelist, Committee on Assessment of Covered Benefits, Expert
2007 - 2010	California Health Benefits Review Program (CHBRP)
2008 - 2011	Center for Scientific Review, NIH, Health Services Organization and Delivery Study Section
2010 - 2011	American Board of Medical Specialties, American Board of Radiology, American College of Radiology, and Physician Consortium for Performance Improvements. Patient Radiation Dose Work Group
2010	Congressional Hearing, US House of Representatives, Energy and Commerce, Subcommittee on Health. Medical Radiation: An Overview of the Issues. Expert Witness
2010	Food and Drug Administration, Center for Devices & Radiological Health, National Meeting Focus on Radiation Safety, Presenter
2010 - 2011	National Quality Forum, Imaging Efficiently Steering Committee
2011 - 2012	Institute of Medicine Committee on Breast Cancer and the Environment, commissioned report "Temporal Changes in Ionizing Radiation and Estimate of Contributions to Breast Cancer," contributing author
2010 - 2011	Lung Cancer Screening with CT Evidence Review Committee. Multidisciplinary collaboration, including American Cancer Society, American College of Chest Physicians; American Society of Clinical Oncology & The National Comprehensive Cancer Network
2011 - 2016	International Council on Radiation Protection (ICRP), Task Group 79 on Defining Effective Dose Use in Medicine
2012	Congressional Hearing, US House of Representatives, Energy and Commerce, Subcommittee on Health, hearing on the Consistency, Accuracy, Responsibility, and Excellence in Medical Imaging and Radiation Therapy (The CARE Bill), Expert Witness
2012	Centers for Disease Control and Prevention, Cancer Prevention Work Group
2012 - 2014	The Joint Commission, Diagnostic Ionizing Radiation and Magnetic Resonance work group focused on issues of safety and guideline development
2013	Government Accountability Office: Medicare Imaging Accreditation Establishing Minimum National Standards and an Oversight Framework to Ensure Quality and Safety of Advanced Diagnostic Imaging Services, May 2013, Contributor
2014	International Atomic Energy Agency (IAEA) United Nations General Assembly and Security Council. Special Committee Considering Impact of Low Dose Radiation
2015	Council of Distinguished Investigators of the Academy of Radiology Research

UNIVERSITY AND PUBLIC SERVICE

Service Narrative

There are several activities to which Dr. Smith-Bindman has contributed. For seven years she participated in the NCI sponsored Physicians Data Query (PDQ), an NCI committee charged with presenting evidenced based, on-line, widely accessible and widely disseminated guidelines relating to cancer screening and diagnosis. She

participated in several activities related to breast cancer screening including acting as a reviewer for the CDC on assessing the guidelines for the National Breast and Cervical Cancer Detection Program, participating in coverage decisions, acting as reviewer and content expert for the CA Health Benefits Review Program analyzing several bills before the state legislature that would expand breast cancer screening to include MRI, and participating in the creation of several IOM Reports. She has participated in several community projects, such as acting on the board of an African American breast cancer advocacy group, and as a consultant to the Metropolitan Breast Cancer Task Force, charged with improving breast cancer mortality rates and racial disparities. During the last five years She has been very active in local, statewide and national efforts around improving radiation safety, including invited presentations to the FDA, testifying before the US Congress on two occasions, working with innumerable societies and government organizations on guidelines and submitting two endorsed quality measures on radiation safety to the National Quality Forum. Her involvement in service activities within the University have focused on increasing the quality and quantity of translational research through participation in several University-wide task forces. Dr. Smith-Bindman serves on several Medical Center Committees, focusing on improved oversight and stewardship around radiation, and projects to improve the efficiency and effectiveness with CT.

UNIVERSITY SERVICE (selected)

2001 - 2015	UCSF School of Medicine, Faculty Recruitment Committees, Radiology, Rad Onc, Medicine
2002	UCSF School of Medicine Dean's Leadership Retreat, Santa Cruz
2003	University of California, Blueprint for Regional Excellence in Breast Cancer Care
2003	UCSF School of Medicine Task Force, Future of UCSF and Mission Bay
2003	UCSF Medical Center, Hospital Exceptional Physician Award, Committee Co-Chair
2003 - 2004	UCSF School of Medicine Task Force, Physician Scientist Program Clinic-Based
2003 - 2005	UCSF School of Medicine Faculty Council
2005	UCSF School of Medicine, Dean's Leadership Retreat, Santa Cruz, CA
2005 - 2006	UCSF Department of Radiology Seminars and Presentation Committee
2005 - 2008	UCSF Department of Radiology Annual Research Symposium Abstract Review Committee
2005 - 2009	UCSF Department of Radiology, SEED Grant Review Committee
2006 - 2007	UCSF Pathways for Clinical and Translational Research
2008 - 2010	UCSF Pathways to Discovery, Clinical and Translational Research, Advisory Council
2007 - 2010	University of California, Office of the President, CA Health Benefits Review Program
2009 - 2017	UCSF, Radiation Safety Committee
2012 - 2014	UCSF Department of Radiology, Maintenance of Certification Committee
2012 - 2015	UCSF Medical Center, Center for Health Care Value
2013 - 2017	UCSF School of Medicine, Conflict of Interest Advisory Committee
2014 - 2016	UCSF Clinical Enterprise, Strategic Plan, Committee for Continuous Process Improvement
2015 - 2017	UCSF Clinical Enterprise, Utilization Management Committee

PUBLIC SERVICE

2003 – 2007	SF Sisters, an African American breast cancer advocacy group, board member
2008 - 2008	Metropolitan Chicago Breast Cancer Task Force, Chicago IL, unpaid consultant
2011 - 2014	National Quality Form, National Consensus Standard for Patient Safety. Measure Developer "UCSF CT Radiation Dose Patient Safety Measure" Measure endorsed
2015	National Quality Forum, Pediatric Measures. Measure Developer, "Pediatric Computed Tomography Radiation Dose" Measure endorsed

TEACHING AND MENTORING

Teaching Narrative

Dr. Smith-Bindman spends substantial time mentoring trainees in clinical research. The trainees have ranged in experience from high school students through mid-career UCSF faculty. The individuals have come from a broad range of departments at UCSF including Radiology, Internal Medicine, Hospital Medicine, Emergency Medicine, Obstetrics and Gynecology, and Urology, and have also come from the UCSF Medical School, The University of California Berkeley, and local SF high schools. On average, she meets with each trainee 1-2 hours per week while collaborating. An NIH Mid-Career Investigator Award (K24) supported her time mentoring these individuals.

She teaches in several formal classes in the department of Epidemiology and Biostatistics primarily targeted to post graduate students who are completing a master's degree in clinical research. She is actively engaged in teaching the Radiology residents and fellows while attending on the clinical service and provides frequent lectures to the Radiology residents focused at research methods; frequently teaches in courses organized by the UCSF Office of Continuing Medical Education for both radiology courses and courses within other medical specialties. The radiology courses focus on using evidence to interpret our studies (usually focused on ultrasound topics), the lectures for other medical specialties focused on how to use imaging more appropriately. As listed above, she also frequently gives grand rounds within UCSF, and nationally on using imaging more appropriately. Lastly, she organized and ran a large, ongoing, virtual symposium on Radiation Safety described below. Both the content and format of this meeting were novel.

TEACHING

Formal scheduled classes for UCSF students.

The first class listed is a course for UCSF Medical Students. The remaining are part of the coursework offered within the UCSF Masters in Clinical Research Program, Department of Epidemiology and Biostatistics

Year	Title	Role	Class Size
2002 - 2005	Epidemiology and Biostatistics, UCSF School of Med	Section Leader	20
2005	Introduction to Diagnostic Testing	Lecturer	18
2007 - 2008	Clinical Performance and Health Outcome Measurement	Lecturer	20
2011 - 2014	Translating Evidence into Policy: Theory and Design	Lecturer	30
2010 - 2015	Framing Research to Influence Policy	Lecturer	25

Post Graduate CME courses (1-5 lectures/meeting)

2001	UCSF Obstetrics and Gynecology Update, San Francisco, CA
2001	UCSF Primary Care Medicine, Aspen, CO
2001	Primary Care Medicine, Maui, HI
2001	Management of the Hospitalized Patient, San Francisco, CA
2001	Controversies in Women's Health, San Francisco, CA
2001	Diagnostic Imaging in Women's Health, San Francisco, CA
2001	MRI & Ultrasound Imaging, Lake Tahoe, CA
2002	Obstetrics and Gynecology Update, San Francisco, CA.
2002	17th Annual Primary Care Medicine: Concepts and Controversies, Aspen, CO
2002	10th Annual Controversies in Women's Health, San Francisco, CA
2002	Diagnostic Imaging in Women's Health, San Francisco, CA
2002	Diagnostic Imaging, Maui, HI
2002	Obstetrical, Gynecological and Abdominal Ultrasound, San Francisco, CA
2003	Primary Care Medicine, Diagnostic Imaging in Women's Health, Maui, HI
2003	11th Annual Controversies in Women's Health, San Francisco, CA
2003	Diagnostic Imaging for Disease Prevention, San Francisco, CA
2003	46th Annual Diagnostic Radiology Postgraduate Course, San Francisco, CA
2003	OB/GYN and Abdominal Ultrasound, San Francisco, CA
2003	MRI and Ultrasound by the Lake, Lake Tahoe, CA
2004	Women's Imaging, Sonoma, CA
2004	Primary Care Medicine, Maui, HI
2004	Diagnostic Imaging in Clinical Practice, San Francisco, CA
2005	Obstetrical and Gynecologic Sonography, San Francisco, CA
2005	Radiology Spring Training, Scottsdale, Arizona
2005	Abdominal Imaging, Montreal and Quebec, Canada
2006	Controversies in Women's Health, San Francisco, CA
2006	Controversies in Breast Cancer Screening and Diagnosis, San Francisco, CA
2006	Cutting Edge Radiology, Diagnosis and Intervention, Vancouver, Canada
2008	Primary Care Medicine: Update 2008, San Francisco, CA
2008	Diagnostic Imaging in Women's Health, San Francisco, CA
2008	Obstetrical/Gynecological and Abdominal Sonography, San Francisco, CA
2009	Primary Care Medicine: Update 2008, San Francisco, CA

2009	Obstetrical/Gynecological and Abdominal Sonography Update, San Francisco, CA
2011	Imaging of Kidney Stones, San Francisco, CA, Director
2011	Primary Care Medicine, Principles & Practice, San Francisco, CA, Keynote
2011	39th Annual Advances in Internal Department of Medicine, San Francisco, CA, Keynote
2011	Controversies in Women's Health, Department of Medicine, San Francisco, CA, Keynote
2012	Updates on Imaging, Maui, Hawaii
2013	UCSF Otolaryngology Annual Conference, San Francisco, CA
2017	UCSF Practical Body Imaging, Kona, Hawaii

Other Teaching

Radiation Safety and CT: Virtual Symposium. Innovative on-line Interactive CME course targeted to physicians (radiologists and those who order imaging), technologists, medical physicists, and trainees. This was created as an on-line, free, virtual meeting focuses on radiation safety. The initial creation of this virtual meeting began in 2013. Creating the meeting involved creating a multidisciplinary, on line, virtual meeting with over 100 lectures (see list of lectures, now offered freely on line - <http://rorl.ucsf.edu/speakers>), 10 live interactive sessions/chat rooms and over 500 registrants enrolled in the meeting during the “live days”, and ongoing attendees attend each month. The speakers at the meeting included numerous department chairs, the director of the Agency for Health Care Policy at the time, a US Congressman, leaders from numerous societies, The Joint Commission, The American Board of Internal Medicine Foundation, and innumerable scientific experts on diverse patient safety issues, and the meeting was an integration of diverse viewpoints and perspectives. Dr. Smith-Bindman directed this meeting and personally wrote and delivered 7 lectures for the meeting. The meeting was novel in format and content.

MENTORING

Pre-doctoral students directly supervised

Dates	Name	Program or School	Current Position
2004 - 2005	C. Kagay	UCSF Medical School	Radiologist, Private Practice
2005 - 2006	A. Ding	UCB/ UCSF MD/MPH	MGH
2005 - 2008	A. Venkatesan	UCSF Medical School	Resident, Stanford
2006 - 2007	E. Dinkelspiel	Urban High School	Student, Univ. of Chicago
2011 - 2015	J. Keegan	Lick Wilmerding High	San Luis Obispo College
2010 - 2015	P. Mehta	UC Berkeley/UCLA Med School	UCLA Medical School
2012 - 2013	J. Zhang	UC Berkeley	Senior
2014 summer	A. Fraser	University High	Georgetown College

Postdoctoral fellows and residents directly supervised

Dates	Name	Position	Current Position
1998 - 2000	M. Copanigro, MD	Radiology Resident / Fellow	Private Practice

1998 - 2000	N. Vincoff, MD	Radiology Resident / Fellow	Private Practice
2003 - 2004	E. Weiss, MD	OB GYN Resident	Private Practice
2003 - 2005	K. Schueler, MD	RORL Research Fellow	Private Practice
2003 - 2005	D. Haggstrom, MD	Internal Medicine Fellow	Indiana University, Faculty
2005 - 2006	K. Reid, MD	Internal Medicine Fellow	Emory Faculty
2005	A. Jensen	PhD student, Copenhagen	Faculty
2005 - 2006	B. Ching, MD	Radiology Fellow	Private Practice,
2005 - 2006	A. Cole, MD	Radiology Fellow	Private Practice
2005 - 2007	L. Goldman, MD	Internal Medicine Fellow	UCSF Faculty
2006 - 2010	J. Lipson, MD	Radiology T32 Scholar	Stanford Faculty
2007 - 2008	J Stengel, MD	Radiology Fellow	Private Practice
2007 - 2008	A. Heath, MD	RORL Research Fellow	Private Practice
2007 - 2009	R. Cho, MD	Radiology Fellow	Private Practice
2007 - 2009	D. Sellami, MD	Radiology Resident / Fellow	Private Practice
2008 - 2009	A. Kamath, MD	Radiology T32 Scholar	NYU Faculty
2009 - 2010	J Ching, MD	OB GYN Resident	Faculty
2009 - 2011	N, Brasic, MD	Radiology Fellow	UCSF Faculty
2010 - 2011	D. Sridhar, MD	Radiology Resident	Private Practice
2010 - 2012	P. Lebda, MD	Radiology Fellow	Cleveland Clinic Faculty
2010 - 2013	I. Burger, MD	Radiology Resident	Private Practice
2010 - 2013	G. Merry, MD	Radiology Resident	Private Practice
2011 - 2014	J. Mongan, MD PhD	Rad Resident / Fellow	UCSF, Faculty
2013 - 2014	S. Hou, MD	Radiology Resident	NYU Faculty
2013 - 2014	C. Lee, MD	Radiology Resident	UCSF Faculty
2013 - 2014	T. Morgan, MD	Radiology Resident	UCSF Faculty
2013 - 2015	LA Hampton, MD	Urology Resident / Fellow	Fellow, Wash U
2013 - 2015	V. Arasu, MD	Radiology Resident	Resident
2013 - 2015	N. Benedetti, MD	Radiology Resident	University of Wash Faculty
2014 - 2015	B Carpenter, MD	Radiology Fellow	UCSF Faculty
2014 - 2015	J. Hsu, MD	Radiology Fellow	Private Practice
2014 - 2018	J. Demb	Epidemiology	UCSF

Faculty Mentoring

Dates	Name	Department / Section	Current Position
2002 - 2005	John Shepherd, MD	Radiology / Musculoskeletal	UCSF, Faculty, Radiology
2004 - 2005	Elaina Curtis, MD	UCSF Visiting Fellow	Univer. of Auckland Faculty
2005 - 2006	John Stein, MD	Emergency Medicine	UCSF Faculty, Emerg Med
2005 - 2006	Max Wintermark, MD	Radiology / Neuro	UVA, Faculty, Radiology
2007 - 2013	Lauren Goldman, MD	Internal Medicine	UCSF, Faculty, Medicine
2008 - 2011	Larry Rand, MD	OBGYN / Maternal Medicine	UCSF, Faculty, OBGYN
2008 - 2014	Antonio Westphalen, MD	Radiology / Abdominal Imaging	UCSF, Faculty, Radiology
2009 - 2017	Liina Poder, MD	Radiology / Abdominal Imaging	UCSF, Faculty, Radiology
2010 - 2018	Ralph Wang, MD	Emergency Medicine	UCSF Faculty, Emerg Med
2014 - 2018	John Mongan, MD, PhD	Radiology / Abdominal Imaging	UCSF, Faculty, Radiology
2014 - 2017	Cindy Lee, MD	Radiology / Abdominal Imaging	UCSF, Faculty, Radiology
2014 - 2017	Tara Morgan, MD	Radiology / Abdominal Imaging	UCSF, Faculty, Radiology
2014 - 2018	Maureen Kohi, MD	Radiology / Interventional	UCSF, Faculty, Radiology
2015 - 2018	Ben Franc, MD PhD	Radiology / Nuclear Medicine	UCSF, Faculty, Radiology
2017 - 2018	Brian Haas MD	Radiology	UCSF, Faculty, Radiology

RESEARCH AND CREATIVE ACTIVITIES

Research Narrative

Dr. Smith-Bindman's research focuses on understanding the impact of diagnostic testing on patient outcomes. She is the director of the UCSF Radiology Outcomes Research Laboratory, and her team includes several programmers, biostatisticians, a developer, and a handful of epidemiologists who serve as project managers for the funded grants below. Her research expertise is in areas of epidemiology, technology assessment, outcomes research, comparative effectiveness research, health services research, and dissemination and implementation sciences focused on imaging. The research has focused on evaluating the quality, utilization, accuracy, predictive values and impact of diagnostic testing on patient health, and has quantified both the risks and benefits of medical imaging when used in different contexts and by different populations. I am leading several studies that assess and standardize the radiation dose used for CT scanning, in order to minimize doses, without loss of diagnostic accuracy. Additional current research is focused on putting systems-based solutions in place to standardize the use of imaging. For example, ongoing projects focus on improving decision support provided to physicians to help improve the use of testing, using evidence to drive and guide the change in practice, and determining the optimal surveillance strategy for the follow up of incidental findings seen on CT imaging. The research projects she leads, listed below, are typically collaborative, involving researchers from diverse clinical areas and who offer diverse methodological expertise.

RESEARCH AWARDS

Current

PI	07/02/2014 - 06/30/2019
NIH	\$1,140,000 direct/yr1
CT DOSE Collaboration: Partnership for Dose	\$7,900,000 total

Collaboration across the US and Europe to standardize and optimize the doses used for CT. The study uses a novel randomized controlled trial design to compare simple feedback to a multicomponent intervention as strategies to optimize doses. There are approximately 125 hospitals participating in the trial.

PI	09/02/2013 - 08/31/2016
PCORI (Patient Centered Outcomes Research Institute)	\$492,163 direct/yr1
CT Radiation Dose Registry to Ensure a Patient Centered Approach for Imaging	\$2,069,365 total

Collaboration across the US and Europe to create benchmarks and standards for CT by pooling data from a large number of hospitals and outpatient facilities

PI	3/01/2015- 02/28/2020
NIH	\$1,834,410 direct/yr1
Risk of Cancer in Childhood Associated with Medical Imaging	\$10,600,000 total

Retrospective cohort across large integrated health care systems to assess imaging in pregnant women and children and to quantify the risk of childhood and adolescent cancer associated with these exposures.

PI (co-PI with Gould, Kaiser Foundation Research)	4/01/2015- 03/30/2020
PCORI	
Pragmatic Trial of More versus Less Intensive Strategies for Surveillance of Patients with Small Pulmonary Nodules	\$14,458,936 total

Prospective comparative effectiveness study across 15 health care systems to compare different strategies for the surveillance of lung nodules. The study is novel in that patients will be recruited with routine clinical care at imaging and the creation of systematic quality improvement strategies to ensure no loss to follow up.

Past

PI	10/01/2010 - 09/30/2013
AHRQ	\$4,830,368 direct/yr1
RCT of US versus CT for Patients with Suspected Renal Colic	\$9,210,000 total

15 Center randomized pragmatic comparative effectiveness trial comparing different strategies for imaging patients with suspected kidney stones. The study exceeded enrollment and follow up targets, and the primary results were published in the NEJM in 2014. Many additional analyses are ongoing using these data.

PI	09/01/2008 - 07/31/2015
NIH K24	\$172,000 direct/yr1
Mid-Career Development Award: Risk of Cancer Associated with Incidental Findings	\$868,632 total

PI	07/01/2011 - 07/01/2014
University of California Office of the President, CHQI	\$250,000 direct/yr1
Standardization and Optimization of CT Radiation Dose	\$750,000 total

Across the University of California Medical Centers.

Five-center observational study to collect radiation data across the five University of California campuses using automated techniques, analyze the sources of variation in dose, and conduct quality improvement initiatives to standardize practice

PI	09/30/2012 - 09/29/2014
CDC (Centers for Disease Control and Prevention)	\$250,000 direct/yr1
PEDS CT-DOSE: Pediatric CT Dose Optimization and Standardization Endeavor	\$500,000 total
<i>Ten center observational study to collect radiation data and create benchmarks in children</i>	

Co-Investigator (PI Solberg, Health Partners)	07/01/2012 - 06/30/2014
PCORI (Patient Centered Outcomes Research Institute)	\$250,000 direct/yr1
Measuring Patient Outcome from High Tech Imaging Studies	\$500,000 total

Mixed methods study to understand imaging use, positive rates of imaging and patient perspectives on imaging, with respect to identifying patient centered outcomes important to patients.

PI	04/01/2009 - 03/31/2011
NIH / R21	\$317,000 total
Risk of Cancer with Incidental Findings Identified on US Imaging	

Retrospective cohort to understand cancer risks of incidental findings

PI	09/01/2008 - 08/31/2010
NIH / R21	\$317,000 total
Radiation Exposure from Imaging: are Doses in a Carcinogenic Range	

Retrospective cohort to understand use of medical imaging within integrated health care systems

PI	10/01/1999 - 07/01/2005
DOD	\$725,515 total
Outcomes of Screening Mammography in Elderly Women	

Medicare Data were analyzed to determine utilization of mammography and factors influencing survival

PI	09/01/1999 - 06/01/2005
NIH K07	\$635,687 total
Outcomes of Screening Mammography in Elderly Women	

NIH Career development award to study breast cancer screening among elderly women.

PI	07/01/2003 - 02/01/2007
California Breast Cancer Research Program	\$583,287 total
Racial Disparity in Breast Cancer Mortality	

Retrospective cohort to understand the causes for racial disparity in breast cancer outcomes

Co-Investigator (PI Kerlikowske UCSF) 04/01/2000 - 03/31/2005
NIH, U01 **\$3,100,000 total**
San Francisco Mammography Registry: A Research Resource

Dr. Smith-Bindman project lead on 1) Physician Predictors of Mammography Accuracy and 2) Validation of the Medicare Screening Algorithm

Co-Investigator (PI – McCune, UCSF) 09/30/2006 - 06/30/2011
NIH
Clinical and Translational Science Institute (CTSI)

The grant is to enhance training and infrastructure across UCSF. I participate in the Biomedical Informatics Program to educate trainees about imaging, epidemiology and study design

Co-Investigator (PI- Lu, UCSF) 04/01/2006 - 03/01/2009
NIH
Statistical Methods for Evaluation and Validation of Tests

Co-Investigator (PI Tlsty, UCSF)) 10/01/2005 - 09/30/2010
NIH
Biological Basis of Breast Density and Breast Cancer Risk

Co-Investigator (PI Esserman, UCSF) 05/01/2003 - 04/30/2007
Department of Defense/USAMRC **\$6,900,000 total**
Blueprint for Regional Excellence in Breast Cancer Care

PI 01/01/2002 - 12/01/2006
Women's Health Research Center, UCSF **\$70,000 total**
Down Syndrome Screening in the US

PI 04/01/2001 - 04/01/2003
Society of Radiologists in Ultrasound **\$40,000 total**
Prenatal Ultrasound for Detection of Birth Defects and Chromosome Abnormalities

PI 04/01/2001 - 04/01/2004
Society of Radiologists in Ultrasound **\$30,000 total**
Physician Variation in Ultrasound Accuracy

PI 07/01/2000 - 06/01/2001 **\$40,000 direct/yr**
Society of North America
U.S. U.K Comparison of The Accuracy of Screening Mammography

P
I 07/07/1999 - 06/01/2000 **\$35,000 direct**
Radiologic Society of North America
Prenatal diagnostic ultrasound for the detection of chromosomal Abnormalities

MOST SIGNIFICANT RESEARCH PUBLICATIONS

- 1) **Smith-Bindman et al. Endovaginal ultrasound to evaluate endometrial abnormalities JAMA 1999**
Vaginal bleeding affects 7% of post-menopausal women, and historically women have undergone an invasive endometrial biopsy to exclude a diagnosis of cancer. This meta-analytic review found that endovaginal ultrasound is an easily tolerated non-invasive test that is accurate for the diagnosis of cancer, so that most women can avoid the need for an endometrial biopsy if they have a normal ultrasound test result. These results have been integrated into clinical practice guidelines in the US, Scotland, England, Germany, and Hong Kong. The publication has been cited 427 times based on SCOPUS accessed in 2015.
- 2) **Smith-Bindman et al. Second-trimester ultrasound to detect fetuses with Down syndrome: a meta-analysis. JAMA. 2001.**
Prenatal ultrasound is widely used to screen for Down syndrome, but the impact on patients has not been well studied. This meta-analytic review suggests that the use of ultrasound for the detection of fetuses affected by Down syndrome may be associated with more harm than benefit, as it can lead to large numbers of unnecessary amniocenteses and subsequent fetal losses with little evidence of benefits. This article was accompanied by extensive media coverage (AP, Reuters, NY Times), and controversy, and prompted discussion regarding the role of ultrasound in prenatal diagnoses. The manuscript has been cited 217 times based on SCOPUS accessed in 2015.
- 3) **Smith-Bindman R et al. US-UK Comparison of Screening Mammography. JAMA 2003.**
Screening mammography is an imprecise test, and there are considerable differences between physicians and programs in the accuracy of screening. This international comparison of screening mammography described 5.5 million mammograms obtained between 1996 to 1999 within three large-scale mammography registries or screening programs. Recall rates and open surgical biopsy rates were twice as high in the U.S. as in the U.K., although cancer rates were nearly identical. There was extensive media coverage (AP, Reuters, NY Times, Wall Street Journal, National Public Radio). These results have been widely cited, and were included in the IOM Report, "Saving Women's Lives." The publication was cited 223 times based on SCOPUS accessed in 2015.
- 4) **Smith-Bindman et al. Physician Predictors of Mammographic Accuracy. J Natl Cancer Inst 2005.**
Beyond the issues raised about the collective quality of mammographic screening in the United States, even more pronounced concern is the glaring variation among U.S. physicians in the ability to accurately interpretation their patients' mammograms. Dr. Smith-Bindman studied the accuracy of mammographic screening among 208 U.S. physicians, who collectively interpreted 1.2 million mammograms, and she found extraordinary variation in the interpretive abilities of radiologists; the sensitivity spanned 29% to 97%, while the false positive rate (the percentage of women who did not have cancer, but who underwent additional diagnostic testing or biopsy at their physician's recommendation) ranged from 1 to 29%. The difference in accuracy was principally due to differences in their training, experience and dedication to screening mammography; in short, the more experienced mammographers - and those who read more than the minimum number of mammograms required by MQSA guidelines - did substantially better. These findings have already been integrated into the Institute of Medicine's report on Mammography Quality Standards, regarding Enhancement of Interpretative Performance. The manuscript was cited 82 times based on SCOPUS accessed in 2015.
- 5) **Smith-Bindman et al. Does Utilization of Screening Mammography Explain Racial and Ethnic Differences in Breast Cancer? Ann Intern Med, 2006**
Racial and ethnic minorities tend to have larger, more advanced stage breast cancers at diagnosis than white women, and African American women have significantly higher breast cancer mortality. It has not been clear, however, if this is due to inherent differences in biology or the utilization of screening mammography. This paper sought to disentangle whether biology or the use of screening was largely responsible for the known racial and ethnic differences in breast cancer. This study was

unique in that detailed cancer information was available from tumor registries that were linked with detailed information regarding mammography utilization. The results were striking. Most of the racial and ethnic differences in breast cancer features were reduced or eliminated after accounting for the frequency of mammography screening. The manuscript was cited 175 times on SCOPUS.

6) **Smith-Bindman et al. Second trimester prenatal ultrasound for the detection of pregnancies at increased risk of Down syndrome. Prenat Diagn 2007** *Prenatal ultrasound is widely used to screen for Down syndrome, but the impact on patients has not been well studied. Our meta-analytic review found that ultrasound was not useful and this prompted our large prospective study which evaluated ultrasound in a larger cohort, including nearly 20,000 women, in whom nearly 500 had fetuses affected by Down syndrome. This large study confirmed these preliminary results. The manuscript was cited 51 times on SCOPUS.*

7) **Smith-Bindman et al. Radiation dose associated with common computed tomography examinations and the associated lifetime attributable risk of cancer. JAMA Internal Medicine 2009** *This paper documented the variation in doses associated with routine CT. The widespread media attention that this paper received contributed to active policy discussion in this area. I was invited to present and discuss the results at the FDA, at a Congressional Hearing sponsored by the Health Subcommittee of the Committee on Energy and Commerce, and innumerable professional society meetings, and submitted (and had endorsed) a measure of quality around CT imaging by the National Quality Forum. The manuscript was cited 857 times based on SCOPUS accessed in 2015.*

8) **Smith-Bindman R, Appendix F. Ionizing Radiation Exposure to the US Population, with a Focus on Radiation from Medical Imaging, in Breast and the Environment: A Life Course Approach. The Institute of Medicine. 2012** *The IOM was commissioned to write a report on environmental causes of breast cancer. The Komen Foundation commissioned the report. I was asked to summarize what is known about the harmful effects of ionizing radiation on breast cancer risks. The IOM concluded that ionizing radiation is one of the largest, and the most preventable causes of breast cancer.*

9) **Miglioretti DL et al. Smith-Bindman senior author. The use of computed tomography in pediatrics and the associated radiation exposure and estimated cancer risk. JAMA Pediatr. 2013** *Using a retrospective cohort design, this paper quantified the use of imaging among children within one of 7 large integrated health care systems, quantified the radiation exposure associated with these examinations, and estimated the likely impact of improved standardization of the conduct of CT on the risks of cancer. The manuscript concluded that if the top outlying radiation exposures could be reduced to the average (a modest goal) that 40% of expected cancer could be eliminated. The manuscript was cited 150 times based on SCOPUS accessed in 2015*

10) **Smith-Bindman R, et al. Risk of Thyroid Cancer based on Thyroid Ultrasound Imaging Characteristic: Result of A Population Based-Study. JAMA Internal Medicine. 2013.** *This retrospective observational study documented the risk of cancer associated with specific thyroid imaging findings. This is the first study that links a large cohort of patients with detailed imaging findings, with a comprehensive tumor registry to permit the quantification of the risk of cancer associated with specific findings. The results suggest that the number of biopsies can be reduced by up to 90%, with a relatively small impact on cancer detected. The results are being rapidly embraced by endocrinologists, surgeons and radiologists.*

11) **Smith-Bindman et al Ultrasound versus Computed Tomography for Suspected Nephrolithiasis NEJM. 2014.** *This 15-center randomized comparative effectiveness study assessed whether ultrasound or CT should be the first imaging test in patients with suspected kidney stones. The study is unique in using a rigorous randomized trial design to assess a diagnostic imaging test, and in assessing a broad range of outcomes other than diagnostic accuracy. Emergency department patients with abdominal pain and suspected nephrolithiasis*

were randomly assigned to one of three arms for imaging: ultrasound performed by an emergency medicine physician, ultrasound provided by a radiologist, or computerized tomography (CT). No significant differences were observed over the next 6 months in rates of severe serious adverse events (SAEs), related SAEs, or total SAEs, or ED or hospital admission rates at 7 or 30 days; however, initial imaging with ultrasound was associated with lower 1 day and 6-month cumulative radiation exposures than initial imaging with CT. The manuscript was cited 45 times based on SCOPUS accessed in 2015

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Current Exposure to Computed Tomography Imaging in US Integrated Health Care Systems, presented at the Conference on Radiation in Health by the Radiation Research Society, Kona, HI, 10/15-17, 2016

Current CT doses from a Computed Tomography Dose Registry in Pediatric Patients, Presented at the American Academy of Pediatrics Annual Meeting, San Francisco, CA, 10/22-25/2017

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Practical Strategies for Optimizing Dose, A Dose of Reality

European Congress of Radiology, European Society of Radiology, 2018
An International Randomized Controlled Trial of Two Interventions for Reducing Doses for Computed Tomography (CT) Through Audit Feedback and Sharing Best Practices

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Exhibit B

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Exhibit C

Rebecca Smith-Bindman Compensation and Prior Testimony

Dr. Smith-Bindman's fees are \$1,000/hr. She has not testified in other cases during the previous four years.

Exhibit 8

Kevin Holcomb, M.D.

Page 1

IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF NEW JERSEY

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IN RE: JOHNSON & :
JOHNSON TALCUM POWDER :
PRODUCTS MARKETING, :
SALES PRACTICES, AND : NO. 16-2738
PRODUCTS LIABILITY : (FLW) (LHG)
LITIGATION :
:
THIS DOCUMENT RELATES :
TO ALL CASES :

- - -

March 27, 2019

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Videotaped deposition of
KEVIN HOLCOMB, M.D., taken pursuant to
notice, was held at Weil Gotshal &
Manges, LLP, 767 Fifth Avenue, New York,
New York, beginning at 9:53 a.m., on the
above date, before Michelle L. Gray, a
Registered Professional Reporter,
Certified Shorthand Reporter, Certified
Realtime Reporter, and Notary Public.

- - -

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Kevin Holcomb, M.D.

Page 2

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Page 3

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Page 5

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Testimony of: KEVIN HOLCOMB, M.D.

By Ms. Garber 12

- - -
E X H I B I T S
- - -

NO.	DESCRIPTION	PAGE
Holcomb-1	Excerpt from the Transcript of Kevin Holcomb, MD, 5/7/18 Page 56	40
Holcomb-2	Excerpt from the Transcript of Kevin Holcomb, MD, 5/7/18 Page 57	45
Holcomb-3	Excerpt from the Transcript of Kevin Holcomb, MD, 5/7/18 Page 103	64
Holcomb-4	IARC Monographs Arsenic, Metals, Fibres And Dusts (Volume 100 C)	71

2 (Pages 2 to 5)

Kevin Holcomb, M.D.

Page 6				Page 8			
1	- - -			1	- - -		
2	EXHIBITS (Cont'd.)			2	EXHIBITS (Cont'd.)		
3	- - -			3	- - -		
4				4			
5	NO. DESCRIPTION PAGE			5	NO. DESCRIPTION PAGE		
6	Holcomb-5 Notice of Oral and 102			6	Holcomb-19 Reports, 344		
7	Videotaped Deposition			7	Prospective Study of		
8	Holcomb-6 Supplemental 110			8	Talc Use and Ovarian		
9	Materials Received			9	Cancer		
10	And Reviewed			10	(Gertig)		
11	& Invoice			11	Holcomb-20 Risk Factors for 363		
12	Holcomb-7 Expert Report of 114			12	Epithelial Ovarian		
13	Kevin Holcomb, M.D.			13	Cancer by		
14	For General Causation			14	Histologic Subtype		
15	Daubert Hearing			15	(Gates)		
16	2/25/19			16	Holcomb-21 Perineal Powder Use 377		
17	Holcomb-8 Talc & Ovarian 180			17	And Risk of Ovarian		
18	Cancer			18	Cancer		
19	(Narod)			19	(Houghton)		
20	Holcomb-9 Table 1 186			20	Holcomb-22 Douching, Talc Use 403		
21	Study Type, Year			21	And Risk of Ovarian		
22	Author Journal			22	Cancer		
23	Holcomb-10 Retire Statistical 199			23	(Gonzalez)		
24	Significance			24	Holcomb-23 Perineal Talc Use 406		
	(Amrhein)				and Ovarian Cancer		
	Holcomb-11 Draft Screening 220				A Systematic Review		
	Assessment				And Metal-Analysis		
	December 2018				(Penninkilampi)		
	Holcomb-12 Systemic Review 224				Holcomb-24 Demonstrative 407		
	and Meta-Analysis				TPP and Ovarian		
	Of the Association				And TPP Serous Cancer		
	Between Perineal				Meta-Analyses		
	Use of Talc and Risk						
	Of Ovarian Cancer						
	(Taher)						
Page 7				Page 9			
1	- - -			1	- - -		
2	EXHIBITS (Cont'd)			2	EXHIBITS (Cont'd)		
3	- - -			3	- - -		
4				4			
5	NO DESCRIPTION PAGE			5	NO DESCRIPTION PAGE		
6	Holcomb-13 Perineal Talc 255			6	Holcomb-25 FDA Letter, 4/1/14 424		
7	Exposure and Epithelial			7	To Epstein from Musser		
8	Ovarian Cancer Risk in			8	RE, Docket Numbers		
9	the Central Valley of			9	JNJ 000489048-54		
10	California			10	Holcomb-26 American Journal of 468		
11	(Mills)			11	Respiratory and		
12	Holcomb-14 Perineal Use of 271			12	Critical Care Medicine		
13	Talc and Risk of			13	Talc Should Not Be Used		
14	Ovarian Cancer			14	For Pleurodeses in		
15	(Langseth)			15	Patients with Nonmalignant		
16	Holcomb-15 Association Between 273			16	Pleural Effusions		
17	Body Powder Use and			17	(Ghio)		
18	Ovarian Cancer:			18	Holcomb-27 Genital Use of Talc 471		
19	The African American			19	And Risk of Ovarian		
20	Cancer Epidemiology Study			20	Cancer: A Meta-Analysis		
21	(AACES)			21	(Berge)		
22	(Schildkraut)			22	Holcomb-28 Epithelial Ovarian 486		
23	Holcomb-16 Six Persistent 281			23	Cancer		
24	Research			24	(Lheureux)		
	Misconceptions				Holcomb-29 What is New in 488		
	(Rothman)				Ovarian Cancer?		
	Holcomb-17 Weill Cornell 292				(Wright)		
	Medicine, Evidence-				Holcomb-30 FDA Advises Consumers 496		
	Based Medicine, EBM				To Stop Using Certain		
	Defined				Claire's Cosmetic		
	(Straus)				Products		
	Holcomb-18 Ovulation and Risk 302				Holcomb-31 Ingredients Talc 503		
	Of Epithelial Ovarian				(FDA Website)		
	Cancer						
	(Purdie)						

3 (Pages 6 to 9)

Kevin Holcomb, M.D.

Page 10	Page 12
<p>1 - - -</p> <p>2 DEPOSITION SUPPORT INDEX</p> <p>3 - - -</p> <p>4</p> <p>5 Direction to Witness Not to Answer</p> <p>6 PAGE LINE</p> <p>7 None.</p> <p>8 Request for Production of Documents</p> <p>9 PAGE LINE</p> <p>10 None.</p> <p>11 Stipulations</p> <p>12 PAGE LINE</p> <p>13 None.</p> <p>14 Questions Marked</p> <p>15 PAGE LINE</p> <p>16 None.</p> <p>17</p> <p>18</p> <p>19</p> <p>20</p> <p>21</p> <p>22</p> <p>23</p> <p>24</p>	<p>1 BY MS. GARBER:</p> <p>2 Q. Good morning, Doctor.</p> <p>3 A. Good morning.</p> <p>4 Q. Would you please state your</p> <p>5 name for the record?</p> <p>6 A. Yes. My name is Kevin</p> <p>7 Holcomb.</p> <p>8 Q. And you're a medical doctor?</p> <p>9 A. Yes, I am.</p> <p>10 Q. Are you a gynecologic</p> <p>11 oncologist?</p> <p>12 A. I am.</p> <p>13 Q. And are you a practicing</p> <p>14 gynecologic oncologist?</p> <p>15 A. I am.</p> <p>16 Q. Where do you practice?</p> <p>17 A. I practice at Weill Cornell</p> <p>18 Medical Center.</p> <p>19 Q. Thank you. Are you here</p> <p>20 today as a litigation expert for the</p> <p>21 defendant, Johnson & Johnson?</p> <p>22 A. I am.</p> <p>23 Q. And this is not the first</p> <p>24 time you've testified for the defendant</p>
Page 11	Page 13
<p>1 - - -</p> <p>2 THE VIDEOGRAPHER: We are</p> <p>3 now on the record. My name is</p> <p>4 Henry Marte. I am a videographer</p> <p>5 with Golkow Litigation Services.</p> <p>6 Today's date is March 27,</p> <p>7 2019, and the time is 9:53 a.m.</p> <p>8 This videotaped deposition</p> <p>9 is being held at 767 Fifth Avenue,</p> <p>10 New York, New York in the matter</p> <p>11 of Talcum Powder Litigation.</p> <p>12 The deponent today is</p> <p>13 Dr. Kevin Holcomb.</p> <p>14 All appearances are noted on</p> <p>15 the stenographic record.</p> <p>16 Will the court reporter</p> <p>17 please administer the oath.</p> <p>18 - - -</p> <p>19 ... KEVIN HOLCOMB, M.D.,</p> <p>20 having been first duly sworn, was</p> <p>21 examined and testified as follows:</p> <p>22 - - -</p> <p>23 EXAMINATION</p> <p>24 - - -</p>	<p>1 Johnson & Johnson regarding their talcum</p> <p>2 powder products and risk of ovarian</p> <p>3 cancer; is that true?</p> <p>4 A. That's true.</p> <p>5 Q. You testified in deposition</p> <p>6 and at trial in the Ingham matter; is</p> <p>7 that correct?</p> <p>8 A. That's correct.</p> <p>9 Q. Have you ever testified in</p> <p>10 deposition or trial in any other talcum</p> <p>11 powder ovarian cancer cases?</p> <p>12 A. No, I haven't.</p> <p>13 Q. Doctor, have you been sued</p> <p>14 in connection with your own medical care</p> <p>15 and treatment?</p> <p>16 A. Yes, I have.</p> <p>17 Q. How many times?</p> <p>18 A. Probably about three.</p> <p>19 Q. Doctor, if you testified in</p> <p>20 a prior matter that it was four times,</p> <p>21 does that refresh your recollection?</p> <p>22 A. It's possible.</p> <p>23 Q. Are all of the matters</p> <p>24 wherein you were sued as a medical</p>

4 (Pages 10 to 13)

Kevin Holcomb, M.D.

Page 14	Page 16
<p>1 defendant resolved in one way or another?</p> <p>2 A. I believe there's still one</p> <p>3 outstanding.</p> <p>4 Q. What is the name of that</p> <p>5 matter?</p> <p>6 A. I'm trying to remember the</p> <p>7 patient's last name. I'm sorry. I don't</p> <p>8 remember the last name of the patient,</p> <p>9 sorry.</p> <p>10 Q. Where was that case venued?</p> <p>11 A. In New York.</p> <p>12 Q. And is it accurate, Doctor,</p> <p>13 that none of those matters concern</p> <p>14 diagnosis and/or treatment of ovarian</p> <p>15 cancer?</p> <p>16 A. That's true.</p> <p>17 Q. Is the nature of the matter</p> <p>18 that's still open in connection with</p> <p>19 performance of robotic surgery?</p> <p>20 A. Yes.</p> <p>21 Q. Thank you. So I don't know</p> <p>22 the last time that you've been deposed.</p> <p>23 Has it been since the Ingham matter?</p> <p>24 A. That was the last time.</p>	<p>1 Q. If you don't understand one</p> <p>2 of my questions, I'm bound to be unartful</p> <p>3 at times, and I don't want you to guess</p> <p>4 at what you think I'm asking you. Just</p> <p>5 please ask me to clarify. Because if you</p> <p>6 don't I'm going to assume that you</p> <p>7 understood my question. Is that fair?</p> <p>8 A. That's fair.</p> <p>9 Q. All right. I just want to</p> <p>10 kind of clear up a few definitions so</p> <p>11 we're on the same page. Okay?</p> <p>12 When I refer to talcum</p> <p>13 powder products today, will you</p> <p>14 understand that that includes Johnson &</p> <p>15 Johnson's Baby Powder and Shower to</p> <p>16 Shower products?</p> <p>17 A. Yes.</p> <p>18 Q. And in your report you use</p> <p>19 the word talc. Is that fair to assume</p> <p>20 that you are including Johnson &</p> <p>21 Johnson's Baby Powder and Shower to</p> <p>22 Shower products?</p> <p>23 MS. CURRY: Objection to</p> <p>24 form.</p>
Page 15	Page 17
<p>1 Q. All right. I'll go through</p> <p>2 the admonitions that typically accompany</p> <p>3 the deposition process so we've reviewed</p> <p>4 the most important ones. Okay?</p> <p>5 A. Okay.</p> <p>6 Q. All right. You've taken an</p> <p>7 oath to tell the truth under penalty of</p> <p>8 perjury. And, Doctor, you understand</p> <p>9 that that oath carries the same force and</p> <p>10 effect as if you were testifying in a</p> <p>11 court of law even though you are in an</p> <p>12 informal setting of this conference room.</p> <p>13 Do you understand that?</p> <p>14 A. I do.</p> <p>15 Q. And you've given depositions</p> <p>16 so you know that the court reporter is</p> <p>17 going to be taking down what's said, and</p> <p>18 we want to avoid talking over one</p> <p>19 another.</p> <p>20 You're doing a good job of</p> <p>21 waiting for my question. And I'll try to</p> <p>22 do the same, wait for your answer, so we</p> <p>23 get a clear record. Okay?</p> <p>24 A. Okay.</p>	<p>1 THE WITNESS: That's true.</p> <p>2 BY MS. GARBER:</p> <p>3 Q. What is a carcinogen?</p> <p>4 A. A carcinogen is something</p> <p>5 that causes cancer.</p> <p>6 Q. What does it mean to be</p> <p>7 carcinogenic?</p> <p>8 A. To have the ability to cause</p> <p>9 cancer.</p> <p>10 Q. What is a risk factor in the</p> <p>11 context of ovarian cancer?</p> <p>12 MS. CURRY: Objection to</p> <p>13 form.</p> <p>14 THE WITNESS: A risk factor</p> <p>15 is something that's associated</p> <p>16 with a higher likelihood of</p> <p>17 developing a cancer.</p> <p>18 BY MS. GARBER:</p> <p>19 Q. How do you define higher</p> <p>20 likelihood?</p> <p>21 A. More likely than if you</p> <p>22 hadn't been exposed.</p> <p>23 Q. To a medical degree of</p> <p>24 certainty?</p>

Kevin Holcomb, M.D.

Page 18	Page 20
<p>1 MS. CURRY: Objection to 2 form. 3 THE WITNESS: Typically that 4 is something that I would relate 5 to statistical analysis from 6 studies. So there would be 7 statistical definitions. 8 BY MS. GARBER: 9 Q. Rather than a medical degree 10 of certainty, correct? 11 MS. CURRY: Objection to 12 form. 13 THE WITNESS: My medical 14 degree of certainty is often based 15 on the statistical results of 16 tests. 17 BY MS. GARBER: 18 Q. How do you define a causal 19 factor in the context of ovarian cancer? 20 A. A causal factor would be 21 something that you know caused the 22 cancer. 23 Q. How do you know if it caused 24 cancer?</p>	<p>1 exposure to a known carcinogen and 2 the development of the cancer that 3 it's associated with, that it 4 causes. 5 BY MS. GARBER: 6 Q. You used the phrase "known 7 carcinogen." How do you know if it's a 8 known carcinogen? 9 A. Well, if it's not a 10 carcinogen, you can't really have a 11 latency period. 12 Q. In the performance of a 13 study assessing whether or not it's a 14 carcinogen, you can nevertheless still 15 have a latency period for purposes of 16 determining follow-up and things of that 17 nature, correct? 18 A. No, I don't think -- 19 MS. CURRY: Objection to 20 form. 21 THE WITNESS: I don't agree 22 with that. 23 BY MS. GARBER: 24 Q. You don't?</p>
Page 19	Page 21
<p>1 MS. CURRY: Objection to 2 form. 3 THE WITNESS: Well, in the 4 context of any individual patient, 5 I can't say what caused their 6 cancer. So I think it's 7 impossible to say on an individual 8 level that you've seen that. 9 Outside of the individual, if you 10 have a substance that can 11 transform cells into a malignant 12 phenotype in a cell culture for 13 example, that would be evidence of 14 a carcinogen. 15 BY MS. GARBER: 16 Q. What is your definition of 17 the phrase latency period in the context 18 of ovarian cancer? 19 MS. CURRY: Objection to 20 form. 21 THE WITNESS: In the context 22 of ovarian cancer -- well, the 23 latency period in any cancer is 24 the time between the initial</p>	<p>1 A. No. 2 Q. All right. Do you have an 3 opinion as to the latency period for 4 ovarian cancer? 5 A. In general, I think to 6 define the latency period, you have to, 7 one, start with a carcinogen, and then 8 have data showing that you have an idea 9 from the time of first exposure to that 10 carcinogen to the development of the 11 disease in question. 12 So latency periods are going 13 to be specific to whichever carcinogen 14 you're speaking about. 15 Q. Okay. Fair enough. Is 16 serous ovarian cancer included under the 17 umbrella of epithelial ovarian cancer? 18 A. It is. 19 Q. So in other words, serous 20 ovarian cancer is ovarian cancer, right? 21 A. It's a type of ovarian 22 cancer, yes. 23 Q. Let's talk about some of 24 your qualifications, okay. Is it</p>

6 (Pages 18 to 21)

Kevin Holcomb, M.D.

<p style="text-align: right;">Page 22</p> <p>1 accurate, Doctor, that you've never 2 conducted research experiments regarding 3 the effects of talcum powder products and 4 its carcinogenicity? 5 A. That's true. 6 Q. And in your CV it shows that 7 you've never published regarding talcum 8 powder products and ovarian cancer, 9 right? 10 A. That's true. 11 Q. Is it also true that you've 12 never published regarding talcum powder 13 products, asbestos, and ovarian cancer? 14 A. That's true. 15 Q. You don't have any 16 publications about asbestos at all, 17 correct? 18 A. That's true. 19 Q. And you don't have any 20 publications with regard to talcum powder 21 products at all, correct? 22 A. That's true. 23 Q. Have you ever created or 24 written any presentations regarding</p>	<p style="text-align: right;">Page 24</p> <p>1 MS. CURRY: Object to the 2 form. 3 THE WITNESS: I'm a little 4 confused by the question. Because 5 if you are giving a lecture and 6 you're listing what you consider 7 risk factors, anything that's not 8 on that list you are not 9 mentioning as a risk factor, so 10 you're -- you're asking me have I 11 formed a negative? 12 BY MS. GARBER: 13 Q. Yeah, well, and I appreciate 14 you asking for clarification, because I 15 don't think my question was a good one, 16 so thank you. 17 I just want to be sure I 18 understand the -- the nature of your 19 presentation. 20 In your presentation you've 21 never actually used the word talc in any 22 of your presentations with regard to risk 23 factors and ovarian cancer; is that true? 24 A. No.</p>
<p style="text-align: right;">Page 23</p> <p>1 talcum powder products and ovarian 2 cancer? 3 A. No. I've created materials 4 on ovarian cancer and its risk factors 5 and general educational information for 6 the students -- medical students, 7 residents and fellows. But not 8 particularly with regard to talc. 9 Q. Did any of -- were those in 10 regard to risk factors and ovarian cancer 11 risk? 12 A. Yes. 13 Q. And did any of those 14 materials address the issue of talc one 15 way or another? 16 A. No. 17 Q. So let me clarify my 18 question. Is it accurate, Doctor, that 19 in those presentations that you've 20 created with regard to risk factors for 21 ovarian cancer, you've never made an 22 affirmative statement in any of those 23 that talc is not a risk factor; is that 24 true?</p>	<p style="text-align: right;">Page 25</p> <p>1 Q. What percentage of your 2 current patients have been diagnosed with 3 female reproductive cancer including 4 ovarian cancer? 5 A. I'd say about 70 percent of 6 my patients have malignant. 7 Q. Can you break that down by 8 way of ovarian cancer? 9 A. Out of that 70 percent, 10 probably 30 percent are ovarian. 11 Q. For the 30 or so percent 12 that have not been diagnosed with a 13 malignancy, do you counsel them with 14 regard to risk factors? 15 MS. CURRY: Objection to 16 form. 17 MS. GARBER: I wasn't done 18 yet. I'll start again. 19 BY MS. GARBER: 20 Q. With regard to the 21 30 percent of your patients that have not 22 been diagnosed with malignancy, is it 23 your custom and practice to counsel them 24 with regard to risk factors for cancer in</p>

Kevin Holcomb, M.D.

<p style="text-align: right;">Page 26</p> <p>1 general?</p> <p>2 MS. CURRY: Objection to</p> <p>3 form.</p> <p>4 THE WITNESS: I take a</p> <p>5 formal history and a complete</p> <p>6 history, and I will address any</p> <p>7 issues that I may bring up. But</p> <p>8 giving a general lecture to each</p> <p>9 patient on the risk factors for</p> <p>10 cancers, it would only come up in</p> <p>11 questions.</p> <p>12 BY MS. GARBER:</p> <p>13 Q. When you take a history,</p> <p>14 Doctor, do you ask for a patient's</p> <p>15 exposure to asbestos?</p> <p>16 A. When I'm taking a history I</p> <p>17 do question patients about their</p> <p>18 occupations. And that would be the only</p> <p>19 thing I can think of where an asbestos</p> <p>20 exposure would likely be revealed.</p> <p>21 Q. Do you know how long it</p> <p>22 takes to conduct an asbestos history?</p> <p>23 MS. CURRY: Object to form.</p> <p>24 BY MS. GARBER:</p>	<p style="text-align: right;">Page 28</p> <p>1 any certain risk of any certain type of</p> <p>2 cancer?</p> <p>3 MS. CURRY: Object to the</p> <p>4 form.</p> <p>5 THE WITNESS: Well, I'm</p> <p>6 aware that heavy occupational</p> <p>7 exposure to asbestos has been</p> <p>8 determined by at least some to be</p> <p>9 a cause of ovarian cancer. So I</p> <p>10 guess if -- if it came out through</p> <p>11 a history that a patient had</p> <p>12 engaged in any of those type of</p> <p>13 practices, it would -- it would</p> <p>14 catch my attention.</p> <p>15 BY MS. GARBER:</p> <p>16 Q. Thank you.</p> <p>17 How many publications do you</p> <p>18 have to your credit about the causes of</p> <p>19 ovarian cancer over your career?</p> <p>20 A. I don't believe any of my</p> <p>21 publications are addressing the causes of</p> <p>22 ovarian cancer.</p> <p>23 Q. Women place talcum powder</p> <p>24 products on their genitals to stay fresh</p>
<p style="text-align: right;">Page 27</p> <p>1 Q. A thorough asbestos history</p> <p>2 of a patient?</p> <p>3 MS. CURRY: Same objection.</p> <p>4 THE WITNESS: No, I don't.</p> <p>5 BY MS. GARBER:</p> <p>6 Q. When you take a history, do</p> <p>7 you ask patients about their exposure to</p> <p>8 talcum powder products?</p> <p>9 A. No.</p> <p>10 Q. Why do you ask them about</p> <p>11 their occupation and put that in the</p> <p>12 context of asbestos?</p> <p>13 MS. CURRY: Object to the</p> <p>14 form.</p> <p>15 THE WITNESS: That's not why</p> <p>16 I'm asking them about the</p> <p>17 occupational history. I was</p> <p>18 thinking, was there any chance of</p> <p>19 asbestos exposure coming up in my</p> <p>20 routine questioning, and I thought</p> <p>21 that would be the only area that I</p> <p>22 could think of it coming up.</p> <p>23 BY MS. GARBER:</p> <p>24 Q. And do you relate that to</p>	<p style="text-align: right;">Page 29</p> <p>1 and clean, right?</p> <p>2 MS. CURRY: Object to the</p> <p>3 form.</p> <p>4 THE WITNESS: I'm not sure</p> <p>5 why every individual uses talcum</p> <p>6 powder.</p> <p>7 BY MS. GARBER:</p> <p>8 Q. Do you understand that women</p> <p>9 place talcum powder products on their</p> <p>10 genitals?</p> <p>11 A. Yes, I do.</p> <p>12 Q. And do you understand that</p> <p>13 women place talcum powder products on</p> <p>14 their body?</p> <p>15 A. Yes, I do.</p> <p>16 Q. And of course, you</p> <p>17 understand that women in the United</p> <p>18 States were likely diapered with talcum</p> <p>19 powder products, correct?</p> <p>20 MS. CURRY: Object to the</p> <p>21 form.</p> <p>22 THE WITNESS: I'm not sure</p> <p>23 of the frequency of using it for</p> <p>24 diaper.</p>

Kevin Holcomb, M.D.

Page 30	Page 32
<p>1 BY MS. GARBER: 2 Q. But you understand that at 3 least some portion of the population in 4 the United States was diapered with 5 talcum powder products, right? 6 A. I do understand that. 7 Q. Are you aware of data that 8 indicates that there are women now with 9 ovarian cancer who use talc on their 10 genitals in the 1950s, '60s, and early 11 1970s? 12 A. Could you repeat the 13 question. 14 Q. Sure. Are you aware of data 15 that indicates that there are women now 16 with ovarian cancer who used talc on 17 their genitals in the 1950s, '60s, and 18 early 1970s? 19 MR. MIZGALA: Object to 20 form. 21 MS. GARBER: Are we -- 22 sorry. Are we going to have one 23 person objecting for the group? I 24 thought that was CMO 11.</p>	<p>1 question. So I'll ask it again. 2 Doctor, are you aware of 3 data that indicates that there are women 4 now with ovarian cancer who used talc on 5 their genitals in the 1950s, '60s, and 6 '70s, any data? 7 MR. MIZGALA: Objection. 8 THE WITNESS: I'm not aware 9 of any specific data, no. 10 BY MS. GARBER: 11 Q. Do you agree generally, 12 Doctor, that there are women now in the 13 United States with ovarian cancer who 14 were diapered with Johnson & Johnson Baby 15 Powder in the 1950s, '60s, and early 16 1970s? 17 MS. CURRY: Object to the 18 form. 19 THE WITNESS: I don't have 20 any specific data on people being 21 diapered in the '50s and '60s. So 22 no, I'd have to say no. 23 BY MS. GARBER: 24 Q. Okay. Johnson & Johnson</p>
Page 31	Page 33
<p>1 MS. SHARKO: No that's not 2 the in the CMO. He doesn't 3 represent J&J. 4 MS. GARBER: I thought I 5 read one objection was for all. 6 MS. SHARKO: Sometimes we do 7 that. 8 BY MS. GARBER: 9 Q. Go ahead, Doctor. I forgot 10 my question. Do you remember it? 11 A. If you would repeat it, I'd 12 appreciate it. 13 Q. Sure. Let me see if you 14 answered it. So my question is, are you 15 aware of data that indicates women now 16 with ovarian cancer who used talcum 17 powder products on their genitals in the 18 early 1950s, '60s, and 1970s? 19 A. I think your question was am 20 I aware of any studies that suggest this. 21 And I'd have to say, I'd have to look 22 through each specific study to see do 23 they mention that in particular. 24 Q. Sure. That wasn't my</p>	<p>1 talcum powder products are cosmetic 2 products, not medications, right? 3 A. That's true. 4 Q. There's no medical benefits 5 for women to use defendant's talcum 6 powder products on their genitals, right? 7 MS. CURRY: Objection to 8 form. 9 THE WITNESS: No, I would 10 disagree with that. 11 BY MS. GARBER: 12 Q. There's medical benefits? 13 MS. CURRY: Object to the 14 form. 15 THE WITNESS: I think you're 16 using a term "medical benefit." 17 I'm not sure if you can first 18 clarify what you mean by medical 19 benefit. 20 BY MS. GARBER: 21 Q. Sure. You've done a 22 risk/benefit assessment of, say, a drug 23 or a medication, right? You know what 24 that means, don't you?</p>

Kevin Holcomb, M.D.

Page 34	Page 36
<p>1 A. I do.</p> <p>2 Q. All right. And what do you</p> <p>3 think that means, when I say a</p> <p>4 risk/benefit in the context of a</p> <p>5 medication?</p> <p>6 A. A risk/benefit would be an</p> <p>7 analysis of the reason why the person is</p> <p>8 using the drug versus the risk of using</p> <p>9 the drug.</p> <p>10 Q. Right. And so the benefit</p> <p>11 is the reason they are using the drug,</p> <p>12 right?</p> <p>13 A. Right.</p> <p>14 Q. It has to have some sort of</p> <p>15 efficacy or benefit, right?</p> <p>16 A. Right.</p> <p>17 MS. CURRY: Object to the</p> <p>18 form.</p> <p>19 BY MS. GARBER:</p> <p>20 Q. So my question is now take</p> <p>21 that to talc and talcum powder products.</p> <p>22 There's no medical benefit</p> <p>23 in that context, is there?</p> <p>24 MS. CURRY: Object to the</p>	<p>1 MS. CURRY: Object to the</p> <p>2 form.</p> <p>3 THE WITNESS: That wasn't --</p> <p>4 no, I wouldn't. But I believe</p> <p>5 your question was, is there a</p> <p>6 medical benefit. And that's in</p> <p>7 the eye of the patient who's using</p> <p>8 it. And I would have to ask her</p> <p>9 why she's using it.</p> <p>10 For example, if someone says</p> <p>11 I'm diabetic, I get yeast</p> <p>12 infections when I'm moist, and I</p> <p>13 find that talcum keeps me dry and</p> <p>14 I have less yeast infections, I</p> <p>15 would say that's probably a</p> <p>16 medical benefit to that</p> <p>17 individual.</p> <p>18 BY MS. GARBER:</p> <p>19 Q. But talcum powder products</p> <p>20 do not fall under the rubric of a</p> <p>21 medication for purposes of regulatory;</p> <p>22 isn't that true?</p> <p>23 A. That's true. But things</p> <p>24 that fall under the rubric of medications</p>
Page 35	Page 37
<p>1 form.</p> <p>2 THE WITNESS: I'm assuming a</p> <p>3 practice that has endured for this</p> <p>4 long of time, there must be a</p> <p>5 perception on the people who are</p> <p>6 using it that they are benefiting</p> <p>7 from it in some form or fashion.</p> <p>8 BY MS. GARBER:</p> <p>9 Q. Sure. My question is a</p> <p>10 little different.</p> <p>11 Is -- is there a medical</p> <p>12 benefit to using talcum powder products</p> <p>13 in the same context as, say, a</p> <p>14 medication, drug, something like that?</p> <p>15 MS. CURRY: Object to the</p> <p>16 form.</p> <p>17 THE WITNESS: Yeah, I would</p> <p>18 say there is.</p> <p>19 BY MS. GARBER:</p> <p>20 Q. There isn't or --</p> <p>21 A. There is, I would say.</p> <p>22 Q. There is? So you would tell</p> <p>23 a patient to use talcum powder products</p> <p>24 for a medical benefit?</p>	<p>1 that we prescribe pretty regularly that</p> <p>2 are just quality of life issues are</p> <p>3 considered medications. I mean there are</p> <p>4 medications that prevent hot flashes. I</p> <p>5 don't believe anybody can point to a</p> <p>6 specific medical benefit of stopping hot</p> <p>7 flashes, but there's still medications</p> <p>8 for that use.</p> <p>9 Q. Doctor, you've been</p> <p>10 designated as an expert by Johnson &</p> <p>11 Johnson in the talcum powder litigation</p> <p>12 in the multi-district litigation; is that</p> <p>13 right?</p> <p>14 A. That's true.</p> <p>15 Q. And you understand that</p> <p>16 we're here today to take your deposition</p> <p>17 to get all your opinions and the bases of</p> <p>18 those opinions so we can prepare for</p> <p>19 briefings, hearings, and trial.</p> <p>20 Do you understand that?</p> <p>21 A. Yes.</p> <p>22 Q. When were you first retained</p> <p>23 in the talcum powder ovarian cancer</p> <p>24 litigation generally, not in the MDL,</p>

10 (Pages 34 to 37)

Kevin Holcomb, M.D.

Page 38	Page 40
<p>1 just in general?</p> <p>2 A. The Ingham case was my only</p> <p>3 other involvement. And I believe that.</p> <p>4 That interaction began late. Probably</p> <p>5 November -- let me think. I guess that</p> <p>6 would be November of 2017 then.</p> <p>7 No, I'm sorry, more like</p> <p>8 January. I think it was more like</p> <p>9 January of 2018 then.</p> <p>10 Q. Were there any documents</p> <p>11 that would refresh your recollection in</p> <p>12 that regard?</p> <p>13 A. Not that I can think of.</p> <p>14 Q. You are not an asbestos</p> <p>15 expert, are you?</p> <p>16 A. No.</p> <p>17 Q. Before you were hired by</p> <p>18 Johnson & Johnson regarding talcum powder</p> <p>19 products, is it fair to say that your</p> <p>20 understanding of asbestos was pretty</p> <p>21 limited?</p> <p>22 MS. CURRY: Object to the</p> <p>23 form.</p> <p>24 THE WITNESS: I'm not sure</p>	<p>1 MS. GARBER: I do.</p> <p>2 BY MS. GARBER:</p> <p>3 Q. Doctor, if I could call your</p> <p>4 attention to --</p> <p>5 MS. GARBER: You know what,</p> <p>6 I am going to mark this as</p> <p>7 Exhibit 1.</p> <p>8 Can I have that back,</p> <p>9 Doctor?</p> <p>10 THE WITNESS: Sure.</p> <p>11 MS. GARBER: Sorry.</p> <p>12 (Document marked for</p> <p>13 identification as Exhibit</p> <p>14 Holcomb-1.)</p> <p>15 BY MS. GARBER:</p> <p>16 Q. I don't mean to throw these</p> <p>17 at you.</p> <p>18 A. I didn't take offense.</p> <p>19 Q. I apologize.</p> <p>20 So the front page of</p> <p>21 Exhibit 1 indicates that this is a</p> <p>22 deposition transcript on May 7th, 2018,</p> <p>23 in the Ingham case; is that correct?</p> <p>24 A. That's correct.</p>
Page 39	Page 41
<p>1 what you mean by limited.</p> <p>2 BY MS. GARBER:</p> <p>3 Q. Did you testify that it was</p> <p>4 pretty limited in a prior case?</p> <p>5 MS. CURRY: Object to the</p> <p>6 form.</p> <p>7 THE WITNESS: When I -- if I</p> <p>8 had used the term limited, I guess</p> <p>9 I was referring to its role in</p> <p>10 gynecologic oncology.</p> <p>11 I'm not an expert in</p> <p>12 asbestos in any way. But I</p> <p>13 probably have the same amount of</p> <p>14 knowledge as anyone else.</p> <p>15 BY MS. GARBER:</p> <p>16 Q. Doctor, let's look at your</p> <p>17 prior testimony, if we can.</p> <p>18 I'm going to mark as</p> <p>19 Exhibit 1 -- no, I'm not going to mark it</p> <p>20 for now.</p> <p>21 Doctor, let me pass you</p> <p>22 over --</p> <p>23 MS. CURRY: Do you have a</p> <p>24 copy of the full transcript?</p>	<p>1 Q. And on the front page it</p> <p>2 indicates that you are the deponent,</p> <p>3 correct?</p> <p>4 A. That I am the?</p> <p>5 Q. Person who was being</p> <p>6 deposed.</p> <p>7 Does your name --</p> <p>8 A. Yes.</p> <p>9 Q. Yes, it is.</p> <p>10 And then, Doctor, if you</p> <p>11 turn to Page 56 of the transcript, lines</p> <p>12 2 through 8, I will read it.</p> <p>13 "Question: In fact, is it</p> <p>14 fair to say that, B, until you began</p> <p>15 consulting for Johnson & Johnson, your</p> <p>16 understanding of the different fibers of</p> <p>17 asbestos that exist was -- was pretty</p> <p>18 limited?</p> <p>19 And then question: "Is that</p> <p>20 fair to say?"</p> <p>21 And the answer was: "That's</p> <p>22 fair to say."</p> <p>23 So, Doctor, you agree that</p> <p>24 your understanding of asbestos was pretty</p>

11 (Pages 38 to 41)

Kevin Holcomb, M.D.

Page 42	Page 44
<p>1 limited before you were hired by J&J, 2 correct? 3 MS. CURRY: Object to the 4 form. 5 THE WITNESS: Your prior 6 question just asked me about my 7 understanding of -- of asbestos 8 and was proceeded by my admitting 9 that I'm not an asbestos 10 specialist. 11 This testimony has to do 12 with my understanding of the 13 different fiber types of asbestos. 14 So I think there's a little bit of 15 a difference in what I was 16 testifying about here and your 17 question. But I don't see the 18 inconsistency. 19 BY MS. GARBER: 20 Q. Okay. Fair enough. 21 As to the fibers, before you 22 were hired by J&J and consulting for 23 them, you weren't even aware what an 24 amphibole was, right?</p>	<p>1 entailed what I thought was 2 necessary to offer an opinion on 3 the question of whether talc use 4 causes ovarian cancer. 5 BY MS. GARBER: 6 Q. At the time that you were 7 hired by Johnson & Johnson to do work in 8 the MDL, you already harbored -- harbored 9 causation opinions based on the work that 10 you did attendant to the Ingham cases, 11 correct? 12 A. That's correct. 13 Q. Isn't it true that in the 14 Ingham case you formed your opinion that 15 talcum powder products do not cause 16 ovarian cancer based on review of 61 17 published studies provided to you by 18 counsel for Johnson & Johnson? 19 MS. CURRY: Object to the 20 form. 21 THE WITNESS: That's -- 22 that's not true. My opinion that 23 talc did not cause ovarian cancer 24 preceded my involvement with</p>
Page 43	Page 45
<p>1 A. No. 2 Q. All right. When were you 3 first retained in the MDL talc 4 litigation? 5 A. That, I believe, was around 6 November of 2018. 7 Q. And what was your 8 understanding of your assignment when you 9 were hired in the MDL? 10 A. My understanding with that, 11 was that I was -- I was being asked for 12 my opinion based on my assessment of the 13 existing body of literature in the area 14 of whether talc causes ovarian cancers. 15 Q. We're going to get to the 16 body of literature in a moment. But were 17 you asked to do anything else? Or 18 what -- strike that. 19 What was your understanding 20 of your assignment? Did it -- did it 21 entail anything else? 22 MS. CURRY: Object to the 23 form. 24 THE WITNESS: I believe it</p>	<p>1 Ingham. 2 But, yes, that reliance list 3 helped further confirm that 4 feeling. 5 (Document marked for 6 identification as Exhibit 7 Holcomb-2.) 8 BY MS. GARBER: 9 Q. Doctor, I'm going to mark as 10 Exhibit 2 another deposition transcript. 11 Doctor, this is -- Exhibit 2 12 is the same front transcript, the Ingham 13 matter, and on your deposition taken on 14 May 7, 2018, right? 15 A. Yes. 16 Q. And at Page 57, Lines 10 17 through 14, question reads: 18 "Are the 61 reliance 19 materials cited in Exhibit 4 the complete 20 universe of the materials that you relied 21 upon in order to form your opinions in 22 that case? 23 "Answer: Yes." 24 Is your testimony different</p>

12 (Pages 42 to 45)

Kevin Holcomb, M.D.

<p style="text-align: right;">Page 46</p> <p>1 today, Doctor?</p> <p>2 MS. CURRY: Object to the</p> <p>3 form.</p> <p>4 THE WITNESS: No, it's not</p> <p>5 any different. The -- I can't</p> <p>6 think of anything that was outside</p> <p>7 of this data that I reviewed for</p> <p>8 this case that I had not seen</p> <p>9 prior.</p> <p>10 My testimony today is that</p> <p>11 my opinion about the causal</p> <p>12 relationship of talc and ovarian</p> <p>13 cancer preceded my involvement in</p> <p>14 Ingham. And your question asked</p> <p>15 me, or you stated in your question</p> <p>16 that my opinion was developed</p> <p>17 during Ingham, or that was my</p> <p>18 understanding of your question.</p> <p>19 And that's all I was trying to</p> <p>20 clarify.</p> <p>21 BY MS. GARBER:</p> <p>22 Q. Your universe of the data</p> <p>23 that you relied on in the Ingham matter</p> <p>24 consisted of 61 published studies</p>	<p style="text-align: right;">Page 48</p> <p>1 opinion in the Ingham case were the</p> <p>2 cohort studies which included gate --</p> <p>3 Gertig, Gates 2010, Houghton, and</p> <p>4 Gonzalez, Heller 1996, and IARC 2010 and</p> <p>5 IARC 2012.</p> <p>6 Is that correct?</p> <p>7 MS. CURRY: Object to form.</p> <p>8 THE WITNESS: No. You're --</p> <p>9 you're piquing my memory of</p> <p>10 this -- of this -- because I</p> <p>11 realize I only have two pages of</p> <p>12 it.</p> <p>13 But repeatedly the counsel</p> <p>14 who was taking my deposition</p> <p>15 attempted to limit, as you are</p> <p>16 defining them, as key pieces of</p> <p>17 information. My -- my opinion was</p> <p>18 based on the totality of all the</p> <p>19 data.</p> <p>20 That -- that answer just did</p> <p>21 not seem acceptable at the time,</p> <p>22 and there was this attempt to</p> <p>23 constantly drill down to me</p> <p>24 identifying a few studies that I</p>
<p style="text-align: right;">Page 47</p> <p>1 provided to you by counsel for J&J.</p> <p>2 MS. CURRY: Object to the</p> <p>3 form.</p> <p>4 BY MS. GARBER:</p> <p>5 Q. Right?</p> <p>6 A. To be honest, some of the</p> <p>7 materials I found on my own. Some of it</p> <p>8 was provided by J&J.</p> <p>9 And again, I -- I don't know</p> <p>10 if you mean to be doing this, but I just</p> <p>11 want to clarify. If I read some of this</p> <p>12 material years ago and had come to an</p> <p>13 independent opinion about this, and then</p> <p>14 I read it again, I don't -- I just want</p> <p>15 to clarify, that my opinion is not being</p> <p>16 made during that case.</p> <p>17 Q. The 61 studies that were</p> <p>18 reflected on a reference list were the</p> <p>19 universe of studies that formed your</p> <p>20 opinion in the Ingham case, correct?</p> <p>21 A. Yes.</p> <p>22 Q. Thank you.</p> <p>23 You testified that the key</p> <p>24 literature that formed the basis of your</p>	<p style="text-align: right;">Page 49</p> <p>1 could say were important, but I</p> <p>2 repeatedly said then and I imagine</p> <p>3 I'll maybe have to do that again</p> <p>4 today, that it is the totality of</p> <p>5 the data that led me to my</p> <p>6 opinion.</p> <p>7 The universe, I believe, as</p> <p>8 you like to call it.</p> <p>9 BY MS. GARBER:</p> <p>10 Q. The totality of the evidence</p> <p>11 that formulated the opinions in this</p> <p>12 matter are listed in the reference list</p> <p>13 of -- lists of your expert report, which</p> <p>14 is dated February 25, 2019, and the</p> <p>15 supplemental reference list.</p> <p>16 Is that a true statement?</p> <p>17 MS. CURRY: Object to the</p> <p>18 form.</p> <p>19 THE WITNESS: That's a true</p> <p>20 statement, but there -- I -- I did</p> <p>21 also read the expert reports of</p> <p>22 others involved in the case. And</p> <p>23 they referenced other papers that</p> <p>24 are not in my reference list.</p>

Kevin Holcomb, M.D.

Page 50	Page 52
<p>1 So I -- I'd have to say I</p> <p>2 came across more than -- than just</p> <p>3 what was in my reference list in</p> <p>4 my preparation.</p> <p>5 BY MS. GARBER:</p> <p>6 Q. And in regard to what you</p> <p>7 just said, reading other experts' reports</p> <p>8 that were involved in the case, is it</p> <p>9 true that you read the experts' report,</p> <p>10 but did not read the underlying studies</p> <p>11 that were referenced in that given expert</p> <p>12 report?</p> <p>13 A. No.</p> <p>14 MS. CURRY: Object to the</p> <p>15 form.</p> <p>16 THE WITNESS: That's exactly</p> <p>17 the opposite of what I'm saying.</p> <p>18 I'm saying at times I would read</p> <p>19 something in an expert report that</p> <p>20 piqued my interest, and I would go</p> <p>21 back and pull that paper and read</p> <p>22 the paper.</p> <p>23 BY MS. GARBER:</p> <p>24 Q. And then you didn't list it</p>	<p>1 that I reviewed the other experts'</p> <p>2 reports and the literature that</p> <p>3 they were basing their opinions</p> <p>4 on, I did in some cases.</p> <p>5 BY MS. GARBER:</p> <p>6 Q. Doctor, you understand that</p> <p>7 I am entitled to know the materials that</p> <p>8 you read, reviewed and relied upon in</p> <p>9 formulating your opinions. You</p> <p>10 understand that, right?</p> <p>11 A. Yes.</p> <p>12 MS. CURRY: I can possibly</p> <p>13 clarify --</p> <p>14 MS. GARBER: I don't --</p> <p>15 MS. CURRY: -- the issue if</p> <p>16 it's helpful.</p> <p>17 MS. GARBER: Let me -- let</p> <p>18 me just finish this line of</p> <p>19 questioning, Ms. Curry. Thank you</p> <p>20 very much.</p> <p>21 BY MS. GARBER:</p> <p>22 Q. And, Doctor, is it your</p> <p>23 testimony that aside from the reference</p> <p>24 lists that are attached to your expert</p>
Page 51	Page 53
<p>1 on your reference list?</p> <p>2 MS. CURRY: Object to the</p> <p>3 form.</p> <p>4 THE WITNESS: It was not</p> <p>5 part of my expert report. My</p> <p>6 expert report had already been</p> <p>7 completed.</p> <p>8 BY MS. GARBER:</p> <p>9 Q. Did you know that a</p> <p>10 supplemental reference list was just</p> <p>11 produced in this matter?</p> <p>12 A. Yes.</p> <p>13 Q. Are you telling me that you</p> <p>14 have reviewed other materials that do not</p> <p>15 appear on any of the reference lists that</p> <p>16 are attached to your expert report or the</p> <p>17 supplemental materials that were just</p> <p>18 produced on the 25th?</p> <p>19 MS. CURRY: Object to the</p> <p>20 form.</p> <p>21 THE WITNESS: I believe that</p> <p>22 it -- I don't know exactly the</p> <p>23 list that you have of everything I</p> <p>24 reviewed. But if it's not clear</p>	<p>1 report and the supplemental materials,</p> <p>2 that there are papers that you have</p> <p>3 reviewed that are not listed there?</p> <p>4 MS. CURRY: Object to the</p> <p>5 form.</p> <p>6 THE WITNESS: I would have</p> <p>7 to review my reference list and</p> <p>8 see what's on there. Or all the</p> <p>9 information that was handed over</p> <p>10 to you as far as what I reviewed.</p> <p>11 But, again, I did look</p> <p>12 through other experts' reports.</p> <p>13 If they referenced a study, in</p> <p>14 most cases, I did not go back and</p> <p>15 review the study. I just read</p> <p>16 what they were saying.</p> <p>17 BY MS. GARBER:</p> <p>18 Q. Can you think of a given</p> <p>19 study that you were reading an expert</p> <p>20 report and it piqued your interest, to</p> <p>21 use your words, and you went and pulled</p> <p>22 it and read it?</p> <p>23 A. No, I can't think of any</p> <p>24 specific papers.</p>

14 (Pages 50 to 53)

Kevin Holcomb, M.D.

Page 54	Page 56
<p>1 MS. GARBER: Go ahead, 2 Ms. Curry. Maybe you can clarify. 3 MS. CURRY: Just to clarify, 4 we have on the supplemental list, 5 in addition to the expert reports, 6 the deposition transcripts and 7 exhibits to the depositions, and 8 so I believe that the additional 9 articles that would have been 10 reviewed by Dr. Holcomb are 11 included in those exhibits. 12 MS. GARBER: I see. So what 13 I'm supposed to do is I'm supposed 14 to go pull the deposition, and 15 pull the exhibits and then move 16 those forward to the reference 17 list to understand his library? 18 MS. CURRY: It's the 19 deposition that you actually took 20 of Dr. Saenz, the exhibits that 21 you presented to her in its 22 totality were provided to 23 Dr. Holcomb after that deposition. 24</p>	<p>1 BY MS. GARBER: 2 Q. Did you prepare the 3 supplemental reference list? 4 A. Yes. I don't remember if 5 there's any overlap I'm saying. 6 Q. Did you type it up yourself? 7 A. No. 8 Q. How was it that that was 9 prepared? 10 A. How was what? 11 MS. CURRY: Object to the 12 form. 13 BY MS. GARBER: 14 Q. The supplemental reference 15 list. 16 A. The lawyers asked me, was 17 there anything else that I had reviewed, 18 and I just gave them a list of which 19 papers I had reviewed. 20 Q. Thank you. What did you do 21 to prepare for today's deposition? 22 A. I reviewed the epidemiologic 23 papers on talc, and in some cases just 24 powder use and ovarian cancer.</p>
Page 55	Page 57
<p>1 BY MS. GARBER: 2 Q. And which of those papers, 3 after reading Dr. Saenz's deposition, 4 which of those -- strike that. 5 Which of those exhibits 6 after reading Dr. Saenz's deposition did 7 you pull and read, if any? 8 A. I didn't have to pull any of 9 them of them. The paper was in the -- in 10 the exhibit. And I don't remember which 11 one. I believe there were about 30 12 exhibits. So if you show me the list I 13 can show you which ones I read. 14 Q. Did you read every single 15 one of them? 16 A. No. 17 Q. Do any come to mind? 18 A. I just said no. 19 Q. Are some of them included in 20 the supplemental reference list that was 21 just produced a couple days ago? 22 MS. CURRY: Object to the 23 form. 24 THE WITNESS: I don't know.</p>	<p>1 I looked at the basic 2 science papers, some that addressed 3 mechanistic questions. 4 I looked at some of the 5 basic science papers on theories of 6 carcinogenesis. 7 I reviewed -- that's pretty 8 much it. I pretty much went through that 9 body of literature, so... 10 Q. The epidemiological 11 literature that you looked at appear on 12 the reference lists that are attached to 13 your expert report and the supplemental 14 reference list that was just produced? 15 A. Yes. 16 Q. And when you say the basic 17 science on mechanism of carcinogenicity, 18 what data are those? 19 MS. CURRY: Object to the 20 form. 21 MS. SHARKO: Can you keep 22 your voice a little louder, 23 please? 24 MS. GARBER: Sure.</p>

15 (Pages 54 to 57)

Kevin Holcomb, M.D.

Page 58	Page 60
<p>1 MS. SHARKO: Thank you.</p> <p>2 THE WITNESS: Could you</p> <p>3 repeat the question as well.</p> <p>4 BY MS. GARBER:</p> <p>5 Q. The basic science with</p> <p>6 regard to mechanism of carcinogenicity,</p> <p>7 what specific studies are those?</p> <p>8 MS. CURRY: Object to the</p> <p>9 form.</p> <p>10 THE WITNESS: I don't</p> <p>11 remember the specific studies</p> <p>12 because most of that came from</p> <p>13 reviewing other experts' expert</p> <p>14 reports.</p> <p>15 BY MS. GARBER:</p> <p>16 Q. Do those studies that you</p> <p>17 reviewed in connection with preparation</p> <p>18 for your deposition appear on the</p> <p>19 reference lists that you have produced?</p> <p>20 A. Again, in those cases I</p> <p>21 wasn't pulling the whole paper. I was</p> <p>22 just reading expert reports. So no, it's</p> <p>23 not.</p> <p>24 Q. When you say science with</p>	<p>1 from the time that you were retained by</p> <p>2 Johnson & Johnson in the MDL through</p> <p>3 today's deposition, you prepared about</p> <p>4 90 hours?</p> <p>5 MS. CURRY: Object to the</p> <p>6 form.</p> <p>7 THE WITNESS: That's true.</p> <p>8 BY MS. GARBER:</p> <p>9 Q. And your pay rate is \$850 an</p> <p>10 hour?</p> <p>11 A. That's true.</p> <p>12 Q. Doctor, in the Ingham case,</p> <p>13 it was your opinion that occupational</p> <p>14 exposure to asbestos couldn't cause</p> <p>15 ovarian cancer; is that correct?</p> <p>16 MS. CURRY: Object to the</p> <p>17 form.</p> <p>18 THE WITNESS: Yes.</p> <p>19 BY MS. GARBER:</p> <p>20 Q. And is that still your</p> <p>21 opinion today?</p> <p>22 A. As with my deposition at the</p> <p>23 time of Ingham, I was quoting IARC's</p> <p>24 monograph on the topic. And also offered</p>
Page 59	Page 61
<p>1 regard to basic science with regard to</p> <p>2 carcinogens, the theories of carcinogens,</p> <p>3 that would be your same answer as the</p> <p>4 prior one; it was in the context of</p> <p>5 reading expert reports?</p> <p>6 A. That's true.</p> <p>7 Q. How many hours did you</p> <p>8 prepare for today's deposition?</p> <p>9 A. Do you mean from the</p> <p>10 beginning of my engagement in the MDL or?</p> <p>11 Q. Specifically in connection</p> <p>12 with just getting ready for today. I'm</p> <p>13 going to get to that, Doctor. And thanks</p> <p>14 for the clarification.</p> <p>15 But just with regard to</p> <p>16 preparing for today's deposition.</p> <p>17 A. I'm not sure -- I asked you</p> <p>18 if there was a difference. But I guess</p> <p>19 in essence there really isn't. I've been</p> <p>20 preparing for this deposition from the</p> <p>21 beginning of my engagement.</p> <p>22 So I would say probably</p> <p>23 about 90 hours.</p> <p>24 Q. So is it your testimony that</p>	<p>1 some critiques of that finding, which</p> <p>2 included concerns about</p> <p>3 misclassification, concerns about whether</p> <p>4 environmental exposures really supported</p> <p>5 the findings or not. And so, you know, I</p> <p>6 spent quite a bit of time in the Ingham</p> <p>7 deposition going through this. But I</p> <p>8 accepted IARC's findings.</p> <p>9 Q. So my question is a little</p> <p>10 narrower.</p> <p>11 A. Mm-hmm.</p> <p>12 Q. Is it your opinion today</p> <p>13 that occupational exposure to asbestos</p> <p>14 can cause ovarian cancer?</p> <p>15 A. In my -- it's my opinion</p> <p>16 that based on the five heavy occupational</p> <p>17 exposure papers cited in that IARC</p> <p>18 monograph, that in those specific</p> <p>19 situations, yes, those exposures did</p> <p>20 contribute to ovarian cancer.</p> <p>21 Q. Doctor, did you testify in</p> <p>22 Ingham that occupational exposure to</p> <p>23 asbestos can cause ovarian cancer?</p> <p>24 MS. CURRY: Object to the</p>

16 (Pages 58 to 61)

Kevin Holcomb, M.D.

Page 62	Page 64
<p>1 form.</p> <p>2 THE WITNESS: Again, if I</p> <p>3 did, it's to the degree of -- I --</p> <p>4 I don't have any opinion outside</p> <p>5 of the literature that I read on</p> <p>6 the topic. And the only</p> <p>7 literature I've read on the topic</p> <p>8 are those five papers cited in the</p> <p>9 monograph. So if I said it during</p> <p>10 Ingham, it's based on the same</p> <p>11 data that I'd be saying it based</p> <p>12 on today.</p> <p>13 BY MS. GARBBER:</p> <p>14 Q. Was it your testimony that</p> <p>15 occupational exposure to asbestos can</p> <p>16 cause ovarian cancer?</p> <p>17 MS. CURRY: Object to the</p> <p>18 form.</p> <p>19 THE WITNESS: I believe so.</p> <p>20 BY MS. GARBBER:</p> <p>21 Q. And is it your opinion today</p> <p>22 that occupational exposure to asbestos</p> <p>23 can cause ovarian cancer?</p> <p>24 MS. CURRY: Object to the</p>	<p>1 in that situation, because the</p> <p>2 question is so broad to say in an</p> <p>3 occupational setting. And I only</p> <p>4 have data on a few different</p> <p>5 settings where it was shown. And</p> <p>6 so I'm going to restrict my</p> <p>7 opinion to the data I've read, and</p> <p>8 the data I've read on those</p> <p>9 specific occupational settings.</p> <p>10 BY MS. GARBBER:</p> <p>11 Q. So, Doctor, I'm going to</p> <p>12 mark as Exhibit 3 --</p> <p>13 (Document marked for</p> <p>14 identification as Exhibit</p> <p>15 Holcomb-3.)</p> <p>16 BY MS. GARBBER:</p> <p>17 Q. -- prior deposition</p> <p>18 testimony in the Ingham matter.</p> <p>19 Doctor, this was deposition</p> <p>20 testimony from May 7, 2018, right?</p> <p>21 A. Yes.</p> <p>22 Q. And if you turn to Page 103,</p> <p>23 Lines 7 through 19, it reads:</p> <p>24 "Question: Do you believe</p>
Page 63	Page 65
<p>1 form.</p> <p>2 THE WITNESS: Once again,</p> <p>3 it's my opinion that occupational</p> <p>4 exposure in those settings as</p> <p>5 described in the IARC monograph,</p> <p>6 which would be, you know, the --</p> <p>7 the women who participated in gas</p> <p>8 mask productions, or cement</p> <p>9 factories in pre-World War II</p> <p>10 Italy, and in those specific</p> <p>11 situations, yes, I think that</p> <p>12 there's enough evidence to deduce</p> <p>13 that -- that exposure increased</p> <p>14 the risk of ovarian cancer.</p> <p>15 BY MS. GARBBER:</p> <p>16 Q. So if I asked you in any</p> <p>17 hearing, Doctor, can occupational</p> <p>18 exposure to asbestos cause ovarian</p> <p>19 cancer, and I asked you for a yes or no</p> <p>20 question, would the answer be yes?</p> <p>21 MS. CURRY: Object to the</p> <p>22 form.</p> <p>23 THE WITNESS: I don't think</p> <p>24 you can ask a yes or no question</p>	<p>1 that asbestos exposure can cause ovarian</p> <p>2 cancer?"</p> <p>3 And your answer is: "Yes.</p> <p>4 We did go over this before and I do</p> <p>5 believe that occupational exposure to</p> <p>6 asbestos can cause ovarian cancer."</p> <p>7 And it goes on to say: "Is</p> <p>8 that because you believe that asbestos</p> <p>9 fibers in the ovaries increases the risk</p> <p>10 of developing ovarian cancer?"</p> <p>11 And your answer was: "I</p> <p>12 have no idea of the mechanism by which it</p> <p>13 could occur."</p> <p>14 Is that still your testimony</p> <p>15 today?</p> <p>16 MS. CURRY: Object to the</p> <p>17 form. And to showing one page of</p> <p>18 the deposition transcript.</p> <p>19 MS. GARBBER: I don't think</p> <p>20 we're going to have any speaking</p> <p>21 objections here today, Ms. Curry.</p> <p>22 I --</p> <p>23 MS. CURRY: It's just --</p> <p>24 you're -- he's referring back to</p>

Kevin Holcomb, M.D.

Page 66	Page 68
<p>1 testimony and you're not showing 2 him the prior testimony. 3 MS. GARBER: As you well 4 know, Ms. Curry, the proper 5 objection is, "Objection to form." 6 MS. SHARKO: I think she's 7 doing fine. 8 MS. GARBER: I'm sure you 9 do. 10 BY MS. GARBER: 11 Q. Go ahead, Doctor. 12 A. So, in my answer I said yes, 13 we did go over this before, which sort of 14 supports the conversation I was saying 15 without all the things I said before, you 16 don't know how to interpret that. 17 But I know what -- how to 18 interpret that. It's what I'm just 19 saying, we had gone over this multiple 20 times being asked the same question, 21 similar to what's happening now. And I 22 kept restricting it to not stepping 23 outside of -- and -- and this is a common 24 theme that I think we're going to revisit</p>	<p>1 that occupational exposure to asbestos 2 can cause cancer. 3 A. Are you -- 4 Q. That's your -- 5 MS. CURRY: Same objections. 6 BY MS. GARBER: 7 Q. That's your answer, right? 8 A. My answer has a piece of it 9 that you can't, or don't, or you're not 10 interested in. And I think it's just as 11 important as the part that you're 12 focusing on that says yes, we did go over 13 this before. 14 I'd be happy to go through 15 the entire transcript of this area. I 16 think you'll find what I'm referring to 17 as being consistent, that I was trying to 18 say that my opinions about exposure in 19 the occupational setting was restricted 20 to the few occupational settings that 21 were defined in the IARC monograph. And 22 that is what I'm trying to tell you now. 23 Because I said we've gone 24 through this before, I'm referring to</p>
Page 67	Page 69
<p>1 over and over today. 2 This idea of making comments 3 and conclusions that go outside of the 4 specific findings of your studies, and 5 purists and careful clinicians and 6 scientists don't do that. And so if you 7 ask me does any occupational exposure 8 increase your risk of asbestos, how would 9 I know? I only have a body of literature 10 that looks at specific situations. And 11 that's the only situation that I'm going 12 to speak to -- speak about. 13 So when I said yes, we did 14 go over this before, that's because this 15 was about who knows how many times I had 16 been asked the same question with the 17 same answer. 18 MS. GARBER: Objection. 19 Motion to strike as nonresponsive. 20 BY MS. GARBER: 21 Q. Doctor, you answered to the 22 question, do you believe that asbestos 23 exposure can cause ovarian cancer, yes. 24 We did go over this. And I do believe</p>	<p>1 those qualifications. 2 Q. I'm just trying to get your 3 opinions here today. You understand 4 that, right? 5 A. I don't. I don't. I don't 6 think so. Because my opinion on this is 7 so clear that I believe that if you're 8 making gas masks in a World War II, or 9 pre-World War II or during World War II 10 factory, or if you're mixing cement in 11 Italy around the same time, that I'd be 12 concerned about your risk of ovarian 13 cancer. 14 Outside of those specific 15 situations, I don't have an opinion. 16 Q. You've read the IARC 17 monograph from 2012 with regard to 18 asbestos, right? 19 A. Yes. 20 Q. And, in fact, it's on your 21 reference list in this matter? 22 A. Yes. 23 Q. And, Doctor, do you think 24 that the IARC 2002 monograph limits risk</p>

18 (Pages 66 to 69)

Kevin Holcomb, M.D.

<p style="text-align: right;">Page 70</p> <p>1 of ovarian cancer to occupational 2 exposure? 3 MS. CURRY: I believe you 4 mean IARC 2012. And objection to 5 form. 6 MS. GARBER: Thank you. 7 BY MS. GARBER: 8 Q. So I'll redo that question. 9 Doctor, do you think the 10 IARC monograph of 2012 limits risk of 11 ovarian cancer to occupational exposure? 12 MS. CURRY: Object to the 13 form. 14 THE WITNESS: I'm telling 15 you my -- my opinion, which is 16 what I think you're trying to get 17 at, is that the only data on 18 occupational exposure that showed 19 an increased risk of ovarian 20 cancer were those same specific 21 settings that I am mentioning to 22 you. And so my personal opinion 23 is that I can only speak towards 24 the relationship of asbestos</p>	<p style="text-align: right;">Page 72</p> <p>1 I just got. So I apologize. 2 BY MS. GARBER: 3 Q. Doctor, if you could turn to 4 Page 219 of the monograph. And, Doctor, 5 you can look up here. It will go quicker 6 this way if you just -- 7 A. I'd rather look at it, if 8 that's okay. 9 You said 219. Oh. 10 Q. Yeah. Why don't you just 11 look up here. I'm just going to read 12 something. 13 219, it says, exposure data, 14 identification of the agent. 15 A. 219 -- but what I saw at the 16 back. 17 Q. Doctor, if you can just look 18 up here. 19 MS. CURRY: I'm sorry. The 20 exhibit that you just handed him 21 does not have a Page 219, is the 22 problem. 23 THE WITNESS: So I just -- I 24 just want to make sure that what</p>
<p style="text-align: right;">Page 71</p> <p>1 exposure in an occupational 2 setting and ovarian cancer with 3 regard to those specific settings. 4 (Document marked for 5 identification as Exhibit 6 Holcomb-4.) 7 BY MS. GARBER: 8 Q. I'm going to mark as 9 Exhibit 4 the IARC monograph of 2012 10 Volume 100-C, titled "Arsenic, Metals, 11 Fibres, and Dust: A Review of Human 12 Carcinogens." 13 And I apologize. I don't 14 have a full copy of this with me. 15 A. Sure. Thank you. 16 MS. SHARKO: Do you have a 17 copy for us? 18 MS. GARBER: That's what I 19 just said, Ms. Sharko. I 20 apologize. I don't have a full 21 copy. I have a page that I'm 22 going to question him from, but 23 not all the pages. 24 It's based on testimony that</p>	<p style="text-align: right;">Page 73</p> <p>1 you've given me is what you're 2 reading. 3 MS. GARBER: Yeah, that's 4 fine. 5 BY MS. GARBER: 6 Q. Why don't you just look up 7 here at the Elmo. 8 A. Are we looking at the same 9 thing? 10 Q. Yes. Yes. I will cure it 11 on the break. 12 MS. SHARKO: If the doctor 13 wants a paper copy, number one 14 he's allowed to have it, and 15 number two -- 16 MS. GARBER: Well, you -- 17 you have one. 18 MS. SHARKO: -- I'm three 19 seats closer to the screen, and I 20 can't even read that. 21 MS. GARBER: You have one, 22 right? 23 MS. SHARKO: So I don't know 24 how he can.</p>

Kevin Holcomb, M.D.

Page 74	Page 76
<p>1 MS. CURRY: This is the one 2 page. I have the full. 3 THE WITNESS: Okay. So -- 4 BY MS. GARBER: 5 Q. So at Page 219, Doctor, do 6 you see that it says asbestos, and then 7 it lists the different fibers, correct? 8 The different types of asbestos? 9 A. I don't know -- can you 10 please -- 11 Q. The title. The title. 12 A. Yes. 13 Q. The top. 14 A. The -- correct. 15 Q. All right. And then under 16 exposure data, Number 1, it says, 17 "Identification of the agent." 18 Do you see that? 19 A. Yes. 20 Q. And then about halfway 21 through the paragraph, it says, "The 22 conclusions reached in this monograph 23 about asbestos and its carcinogenic 24 risk" --</p>	<p>1 this monograph about asbestos and its 2 carcinogenic risks apply to these six 3 types of fibers wherever they are found." 4 And I'm going to assume that the 5 conclusions are going to be based on the 6 studies that they cite. 7 Q. Doctor, we don't want to 8 make conclusions. My question is, does 9 that what the monograph say? 10 A. That's what the monograph -- 11 Q. Did I read that correctly? 12 A. You read the monograph 13 correctly. 14 Q. And I have no further 15 question for you. 16 MS. GARBER: Motion to 17 strike everything besides saying 18 yes, that's what it says. 19 MS. SHARKO: Does that mean 20 that we're done for today? 21 BY MS. GARBER: 22 Q. Doctor, is that what the 23 monograph says on Page 219? 24 A. That's what the monograph</p>
Page 75	Page 77
<p>1 A. I'm sorry. I'm still just 2 getting up to where you are. 3 Q. Just look -- just look up at 4 here, Doctor. 5 A. Ma'am, if it's okay with 6 you, we went through the trouble to get 7 this because it's easier for me to see. 8 I'm going to use this if you just bear 9 with me. 10 Q. Okay. Well, then you can 11 look up here to see where I'm reading. 12 A. I've got you. 13 Q. Okay. "The conclusions 14 reached in this monograph about asbestos 15 and its carcinogenic risks apply to these 16 six types of fibers wherever they are 17 found, and that includes talc containing 18 asbestiform fibers." 19 Correct? Is that what it 20 says? 21 A. That's what it says. 22 Q. Doctor, that's my only 23 question. Is that what it says? 24 A. "The conclusions reached in</p>	<p>1 says. I disagree with that. Yes. 2 Q. Okay. What part do you 3 disagree with? 4 MS. CURRY: Object to the 5 form. 6 THE WITNESS: I think -- I 7 was getting at this before, and I 8 think that a lot of what we're 9 going to get into today makes that 10 same mistake. You can't make 11 conclusions about things that you 12 haven't studied. And if you only 13 study a certain setting, and 14 you're able to show that in this 15 setting it causes ovarian cancer, 16 how can you reliably expand that 17 finding to situations that you've 18 never even looked at? 19 And I don't care if IARC 20 puts it in writing and says they 21 are going to do that. The 22 question is, do I accept that? Do 23 I accept that if you show me that 24 it causes cancer if you're making</p>

20 (Pages 74 to 77)

Kevin Holcomb, M.D.

Page 78	Page 80
<p>1 gas masks, that means it causes</p> <p>2 cancer in any other situation.</p> <p>3 I think that's -- clearly is</p> <p>4 what IARC said they did. I think</p> <p>5 that's a problem. And I already</p> <p>6 explained to you some of the other</p> <p>7 issues that I have with IARC. I</p> <p>8 mean, we all can make mistakes.</p> <p>9 There's other issues with IARC. I</p> <p>10 mean, the studies, even in the</p> <p>11 ones that I accept, there's</p> <p>12 misclassification issues.</p> <p>13 In fact, if you look at the</p> <p>14 studies where they do pathologic</p> <p>15 confirmation, the increased risk</p> <p>16 is attenuated to the baseline.</p> <p>17 And so, you know, part of my</p> <p>18 being able to give my opinion here</p> <p>19 is my years of practice. And I've</p> <p>20 had the experience of debulking</p> <p>21 somebody who I thought had ovarian</p> <p>22 cancer who ended up having</p> <p>23 mesothelioma.</p> <p>24 So I know the difficulties</p>	<p>1 settings where they found that</p> <p>2 it's associated with, there are</p> <p>3 weaknesses in their findings. To</p> <p>4 extend that definition outside to</p> <p>5 any occupational exposure that</p> <p>6 they haven't examined, I think is</p> <p>7 problematic.</p> <p>8 BY MS. GARBER:</p> <p>9 Q. Doctor, what was my</p> <p>10 question?</p> <p>11 A. Did IARC make that</p> <p>12 statement, and I said yes.</p> <p>13 Q. Thank you.</p> <p>14 MS. GARBER: Motion to</p> <p>15 strike everything besides that.</p> <p>16 MS. SHARKO: Well, that</p> <p>17 wasn't the question you asked.</p> <p>18 BY MS. GARBER:</p> <p>19 Q. Doctor, you disagree --</p> <p>20 MS. CURRY: He answered your</p> <p>21 question.</p> <p>22 MS. O'DELL: All right,</p> <p>23 Susan. We went over this</p> <p>24 earlier -- I think -- not earlier</p>
Page 79	Page 81
<p>1 in being able to tell the</p> <p>2 difference between the two.</p> <p>3 BY MS. GARBER:</p> <p>4 Q. Doctor, I'm going to get to</p> <p>5 your report.</p> <p>6 MS. CURRY: Were you</p> <p>7 finished with your response?</p> <p>8 THE WITNESS: No.</p> <p>9 And I'm also aware that, you</p> <p>10 know, there was not even a</p> <p>11 diagnosis code for malignant</p> <p>12 mesothelioma at a time that -- an</p> <p>13 international diagnosis code, an</p> <p>14 ICD-9 code for mesothelioma during</p> <p>15 this time.</p> <p>16 And I'm sure that the</p> <p>17 immunohistochemical test that</p> <p>18 helped to distinguish between</p> <p>19 ovarian cancer and primary</p> <p>20 peritoneal cancer and malignant</p> <p>21 mesothelioma were not developed at</p> <p>22 that time.</p> <p>23 So, yes, I take IARC at what</p> <p>24 they're saying. But even in the</p>	<p>1 this week, last week. I think</p> <p>2 Dawn is doing the objections.</p> <p>3 There's no need for you to add the</p> <p>4 commentary.</p> <p>5 MS. SHARKO: Well, why --</p> <p>6 why are you talking if it's one</p> <p>7 lawyer per side? You should have</p> <p>8 been there yesterday when you had</p> <p>9 three people on your side talking</p> <p>10 at us.</p> <p>11 MS. O'DELL: Well, I</p> <p>12 can't -- can't speak to yesterday.</p> <p>13 But we've had this discussion, you</p> <p>14 and I, and --</p> <p>15 MS. CURRY: As the person</p> <p>16 making objections, I do want to</p> <p>17 put on the record that the</p> <p>18 question that was asked was what</p> <p>19 part of -- of IARC do you disagree</p> <p>20 with, and so Dr. Holcomb's</p> <p>21 response was directly responsive</p> <p>22 to that question.</p> <p>23 Thank you.</p> <p>24</p>

21 (Pages 78 to 81)

Kevin Holcomb, M.D.

Page 82	Page 84
<p>1 BY MS. GARBER: 2 Q. Doctor, we will get to your 3 report and what you say about asbestos. 4 My question was simply, 5 Number 1, at Page 219 where I read: "Is 6 that what the monograph says?" 7 And I think your testimony 8 was, yes, that's what the monograph says, 9 correct? 10 A. That's what the monograph 11 says. 12 Q. All right. And then I 13 wanted to show you next at Page 232 with 14 regard to your testimony about the 15 populations? 16 A. I'm sorry. 17 Q. 232 -- 18 A. 232, right. 19 Q. -- under human exposure. 20 A. This is the -- 21 Q. Are you there? 22 A. I'm just a little confused, 23 because this is talking about talc. And 24 we were talking about asbestos.</p>	<p>1 it says. 2 It says, "Consumer products, 3 e.g., cosmetic, pharmaceuticals, are the 4 primary sources of exposure to talc for 5 the general population. Inhalation and 6 dermal contact through" -- "i.e., through 7 perineal application of talcum powders, 8 are the primary routes of exposure." 9 Did I read that correctly? 10 A. Yes. 11 Q. So that is indicating that 12 talcum powder products and exposure in 13 the general population, correct? 14 MS. CURRY: Object to form. 15 BY MS. GARBER: 16 Q. That's on Page 232? 17 A. I -- I just want to -- I 18 know we're only picking out this one page 19 to read, but it's a little confusing to 20 me since we had started reading a 21 monograph on asbestos and this seems to 22 be dealing with talc. 23 So I turn one page back. 24 This is a section on talc containing</p>
Page 83	Page 85
<p>1 Are we in the same -- 2 Q. Are you -- 3 A. I think I'm in a 4 different -- 5 Q. -- are you on Page 232? 6 A. Yes, but I don't know if I'm 7 reading the same thing you are. You are 8 talking about the monograph on -- 9 Q. On asbestos. 10 A. Right. I think I'm in the 11 wrong -- 12 Q. No, that is -- that is -- 13 A. This is the right one? Oh, 14 2012. So this is the one. 15 Q. Okay. Doctor, under 1.6.5, 16 it says, "Human Exposure"? 17 A. Yeah. 18 Q. And then it indicates 19 "Exposure of the General Population." 20 Is that the heading? 21 A. Exposure of the general 22 population. And it's -- yeah, exposure 23 to talc for the general population. 24 Q. Okay. Well, let's read what</p>	<p>1 asbestiform fibers. 2 So this area that we are 3 talking about -- I -- I don't know if 4 they are talking about -- what -- I'm a 5 little unclear of what they are talking 6 about here, with the general -- are they 7 talking about asbestiform fibers? Are 8 they talking about -- I'm not sure. 9 Q. Let me see if I can help 10 you. 11 A. Thank you. 12 Q. So turning back to 219. 13 A. Yes. 14 Q. Where the monograph says, 15 "The conclusions reached by the monograph 16 about asbestos and its carcinogenic risks 17 apply to these six types of fibers 18 wherever they are found -- thereby 19 meaning asbestos -- and that includes 20 talc containing asbestiform fibers." 21 So this monograph applies to 22 both talc containing asbestiform fibers, 23 and asbestos. 24 You understand that,</p>

Kevin Holcomb, M.D.

Page 86	Page 88
<p>1 correct?</p> <p>2 A. This goes to the question of</p> <p>3 what I disagree with, because what you're</p> <p>4 saying is that if they study asbestos in</p> <p>5 these heavy occupational exposures, that</p> <p>6 means you should then extend these</p> <p>7 findings to other clinical settings</p> <p>8 outside of that. And -- so yes, I get</p> <p>9 what you're saying and that's exactly</p> <p>10 what I was saying I disagreed with.</p> <p>11 Q. Do you -- I guess I don't</p> <p>12 know what your -- what your opinion is,</p> <p>13 so I'll ask it.</p> <p>14 You understand that this</p> <p>15 monograph from 2012 applies to asbestos</p> <p>16 and asbestiform talc, you understand</p> <p>17 that, right?</p> <p>18 A. Yes.</p> <p>19 Q. Thank you.</p> <p>20 Doctor, in your expert</p> <p>21 report and just a minute ago, you were</p> <p>22 talking about the misdiagnosis of ovarian</p> <p>23 cancer and peritoneal mesothelioma. Do</p> <p>24 you recall that?</p>	<p>1 testifying a bit ago, right?</p> <p>2 A. That's true.</p> <p>3 Q. All right. But it goes on,</p> <p>4 doesn't it, Doctor? It says, "The</p> <p>5 conclusion received" -- "the conclusion</p> <p>6 received additional support from studies</p> <p>7 showing that women and girls with</p> <p>8 environmental, but not occupational</p> <p>9 exposure to asbestos," right?</p> <p>10 A. This is what I was --</p> <p>11 maybe -- maybe it wasn't clear what I was</p> <p>12 referring to when you asked me earlier</p> <p>13 what I disagreed with.</p> <p>14 And I talked about the</p> <p>15 limitations of the IARC monograph. I</p> <p>16 mentioned this issue, that they'll make</p> <p>17 these statements and then they give you a</p> <p>18 couple of papers to go look at; Ferante,</p> <p>19 et al., and Reid, et al.</p> <p>20 When you go back and you</p> <p>21 look at those studies, they actually come</p> <p>22 to the exact opposite conclusion, that</p> <p>23 women in those settings did not have an</p> <p>24 increased risk of ovarian cancer. And</p>
Page 87	Page 89
<p>1 A. I said misclassification.</p> <p>2 Q. Okay. And, we'll turn to</p> <p>3 that part of your expert report in a bit.</p> <p>4 But since you brought it up, if you could</p> <p>5 turn to Page 356 of the monograph.</p> <p>6 A. Sand and gravel?</p> <p>7 Q. It's -- did I say three?</p> <p>8 A. You said 356, sand and</p> <p>9 gravel.</p> <p>10 Q. 256. I apologize.</p> <p>11 A. Okay.</p> <p>12 Q. Okay. If you look at the</p> <p>13 right-hand column. We'll -- we'll start</p> <p>14 with the first full paragraph which reads</p> <p>15 the working group -- are we together?</p> <p>16 A. Yes.</p> <p>17 Q. Okay. "The working group</p> <p>18 noted that a causal association between</p> <p>19 exposure to asbestos and cancer of the</p> <p>20 ovary was clearly established based on</p> <p>21 five strongly positive cohort mortality</p> <p>22 studies of women with heavy occupational</p> <p>23 exposure."</p> <p>24 That's what you were</p>	<p>1 yet the IARC authors say that their</p> <p>2 findings were supported. So they have</p> <p>3 five strong studies showing an increased</p> <p>4 risk of ovarian cancer. Two studies</p> <p>5 in -- in environmental settings that show</p> <p>6 no increases of ovarian cancer come to</p> <p>7 the conclusion that that is not a</p> <p>8 discrepancy, it's actually in support of.</p> <p>9 And I am supposed to read</p> <p>10 this and agree with that.</p> <p>11 Q. You disagree with IARC and</p> <p>12 their findings with regard --</p> <p>13 A. No, and if they regard --</p> <p>14 Q. Hold on, Doctor.</p> <p>15 A. Yes. Okay.</p> <p>16 Q. You disagree with IARC and</p> <p>17 their findings with regard to asbestos</p> <p>18 and asbestiform talc and its</p> <p>19 carcinogenicity as it relates to the</p> <p>20 ovary, correct?</p> <p>21 MS. CURRY: Object to the</p> <p>22 form.</p> <p>23 THE WITNESS: My opinion</p> <p>24 about this is that I restrict my</p>

23 (Pages 86 to 89)

Kevin Holcomb, M.D.

Page 90	Page 92
<p>1 opinions about the carcinogenicity</p> <p>2 of asbestos with ovarian cancer to</p> <p>3 the settings where it was shown to</p> <p>4 increase ovarian cancer.</p> <p>5 If you ask me about settings</p> <p>6 where the studies explicitly show</p> <p>7 it did not increase ovarian</p> <p>8 cancer, I don't accept that it</p> <p>9 increases ovarian cancer in those</p> <p>10 situations.</p> <p>11 I don't understand how a</p> <p>12 reasonable person could. If you</p> <p>13 read a study that says it did not</p> <p>14 increase risk of ovarian cancer in</p> <p>15 a situation, why would you then</p> <p>16 conclude that it does?</p> <p>17 BY MS. GARBER:</p> <p>18 Q. Have you done a thorough and</p> <p>19 comprehensive assessment of the</p> <p>20 literature as it pertains to asbestos and</p> <p>21 ovarian cancer?</p> <p>22 MS. CURRY: Object to the</p> <p>23 form.</p> <p>24 THE WITNESS: To be honest,</p>	<p>1 form.</p> <p>2 THE WITNESS: I believe I</p> <p>3 have. I'm disagreeing with you.</p> <p>4 BY MS. GARBER:</p> <p>5 Q. Because --</p> <p>6 A. I'm saying --</p> <p>7 Q. Because you --</p> <p>8 A. -- because I reviewed</p> <p>9 IARC --</p> <p>10 MS. CURRY: Sorry. You</p> <p>11 can't talk over one another.</p> <p>12 Do you want to finish your</p> <p>13 response?</p> <p>14 THE WITNESS: My</p> <p>15 understanding is that IARC,</p> <p>16 because so many other groups rely</p> <p>17 on their findings to inform their</p> <p>18 opinions, that they are tasked</p> <p>19 with doing a comprehensive review</p> <p>20 of the literature on the topic.</p> <p>21 And so yes, I feel like if I</p> <p>22 reviewed what they reviewed, I've</p> <p>23 done a comprehensive review as</p> <p>24 well.</p>
Page 91	Page 93
<p>1 I'm hoping that IARC would have</p> <p>2 done an extensive study of the</p> <p>3 literature. So my only -- as I've</p> <p>4 already admitted, I'm not an</p> <p>5 asbestos specialist, so my</p> <p>6 understanding of asbestos and</p> <p>7 ovarian cancer is limited to IARC.</p> <p>8 And if they've done an</p> <p>9 extensive review to reach their</p> <p>10 conclusions, then I would have to</p> <p>11 say that I have as well, because I</p> <p>12 reviewed the papers they've</p> <p>13 reviewed. And I've already</p> <p>14 repeatedly told you the problems</p> <p>15 that I have with saying you're</p> <p>16 supported by studies that find the</p> <p>17 exact opposite findings of the</p> <p>18 studies that hold your original</p> <p>19 opinion.</p> <p>20 BY MS. GARBER:</p> <p>21 Q. Is the answer to my question</p> <p>22 no, I have not conducted a full</p> <p>23 comprehensive review of the literature?</p> <p>24 MS. CURRY: Object to the</p>	<p>1 BY MS. GARBER:</p> <p>2 Q. With regard to the</p> <p>3 misclassification issue that you</p> <p>4 testified about, Doctor, if you could</p> <p>5 look back at Page 256.</p> <p>6 A. Yes.</p> <p>7 Q. It indicates, "The working</p> <p>8 group carefully considered the</p> <p>9 possibility that cases of peritoneal</p> <p>10 mesothelioma may have been misdiagnosed</p> <p>11 as ovarian cancer and that these</p> <p>12 contributed to the observed excesses.</p> <p>13 Contravening that possibility is the</p> <p>14 finding that three of the studies cited</p> <p>15 here specifically examined the</p> <p>16 possibility, and there were misdiagnosed</p> <p>17 cases of peritoneal mesothelioma, and all</p> <p>18 failed to find sufficient numbers of</p> <p>19 misclassified cases."</p> <p>20 Doctor, do you agree with</p> <p>21 that statement?</p> <p>22 A. I agree with the statement</p> <p>23 that they did not find what they</p> <p>24 considered enough cases of misclassified</p>

24 (Pages 90 to 93)

Kevin Holcomb, M.D.

Page 94	Page 96
<p>1 cases. But I'm aware that they actually</p> <p>2 did not go back and do a histologic</p> <p>3 evaluation of every case.</p> <p>4 What I'm also aware of is</p> <p>5 that specific cases that do</p> <p>6 systematically go back and have</p> <p>7 pathologic confirmation somehow come to a</p> <p>8 different conclusion than the studies</p> <p>9 that don't do that. And so I'm still</p> <p>10 left wondering, if you do a systematic</p> <p>11 pathology review and classify them, you</p> <p>12 don't find an increased risk. If you</p> <p>13 don't do a systematic pathology</p> <p>14 confirmation, you find an increased risk.</p> <p>15 I'm like IARC, I'm not</p> <p>16 convinced that misclassification has been</p> <p>17 totally ruled out because I can't</p> <p>18 understand why these two different types</p> <p>19 of studies are coming -- you see, you're</p> <p>20 losing consistency then.</p> <p>21 Q. IARC found otherwise.</p> <p>22 A. I just admitted that I have</p> <p>23 a different opinion.</p> <p>24 Q. So your review as to the</p>	<p>1 A. Yes.</p> <p>2 Q. And asbestiform talc?</p> <p>3 A. Yes.</p> <p>4 Q. Thank you.</p> <p>5 Do you agree, Doctor, that</p> <p>6 asbestos and asbestiform talc are Group 1</p> <p>7 carcinogens under IARC 2012?</p> <p>8 A. I agree.</p> <p>9 Q. Doctor, if talcum powder</p> <p>10 products contain asbestos, talcum powder</p> <p>11 products contain a Group 1 carcinogen?</p> <p>12 MS. CURRY: Object to the</p> <p>13 form.</p> <p>14 THE WITNESS: Excuse me?</p> <p>15 BY MS. GARBER:</p> <p>16 Q. You just testified that</p> <p>17 asbestos is a Group 1 carcinogen, right?</p> <p>18 A. Yes.</p> <p>19 Q. And --</p> <p>20 A. According to IARC, yes.</p> <p>21 Q. Okay. And if, it's a</p> <p>22 hypothetical, talcum powder products</p> <p>23 contain asbestos, then those talcum</p> <p>24 powder products contain a Group 1</p>
Page 95	Page 97
<p>1 issue of asbestos and asbestiform talc</p> <p>2 and carcinogenicity is limited to IARC</p> <p>3 2012, correct?</p> <p>4 MS. CURRY: Object to the</p> <p>5 form.</p> <p>6 THE WITNESS: Again, I'm</p> <p>7 trying to -- trying to state this</p> <p>8 as clearly as possible so we can</p> <p>9 move on.</p> <p>10 My opinion of asbestos and</p> <p>11 its ability to cause cancer of the</p> <p>12 ovary are restricted to the</p> <p>13 studies of heavy occupational</p> <p>14 exposure in which they actually</p> <p>15 found an increased risk of ovarian</p> <p>16 cancer.</p> <p>17 BY MS. GARBER:</p> <p>18 Q. And your review to come to</p> <p>19 your opinions is limited to IARC 2012?</p> <p>20 MS. CURRY: Object to form.</p> <p>21 THE WITNESS: As far as</p> <p>22 asbestos?</p> <p>23 BY MS. GARBER:</p> <p>24 Q. Yes.</p>	<p>1 carcinogen, right?</p> <p>2 A. That would be IARC's</p> <p>3 opinion, yes.</p> <p>4 Q. Is it your opinion? It's a</p> <p>5 Group 1 carcinogen.</p> <p>6 A. You asked, you asked what --</p> <p>7 in the beginning whether -- what's my</p> <p>8 definition of a carcinogen. And I said</p> <p>9 it's a substance that can cause cancer.</p> <p>10 So on one hand you're asking</p> <p>11 if it contains this substance that IARC</p> <p>12 has deemed a Level 1 carcinogen, would it</p> <p>13 contain that carcinogen? By definition,</p> <p>14 yes. You said if I take that</p> <p>15 supposition.</p> <p>16 I would just say I'm looking</p> <p>17 at, and I was asked to review the</p> <p>18 literature on talc. And you asked me</p> <p>19 what do I consider talc, and I said</p> <p>20 Johnson & Johnson and Shower to Shower.</p> <p>21 Is that a carcinogen?</p> <p>22 And now that goes back to my</p> <p>23 definition of carcinogen. Can that</p> <p>24 powder cause cancer? And my review, as</p>

25 (Pages 94 to 97)

Kevin Holcomb, M.D.

Page 98	Page 100
<p>1 you know you've already asked, would be</p> <p>2 no.</p> <p>3 Q. Well, so I'll go back to my</p> <p>4 question.</p> <p>5 Assume that talcum powder</p> <p>6 products contain asbestos, then they</p> <p>7 contain a Group 1 carcinogen, right?</p> <p>8 MS. CURRY: Object to form.</p> <p>9 THE WITNESS: You know,</p> <p>10 we're sort of tying all these</p> <p>11 things together. I already</p> <p>12 explained that I disagreed with</p> <p>13 IARC's definition of at least its</p> <p>14 role of -- outside of those heavy</p> <p>15 occupational exposures, which are</p> <p>16 the only studies that they cite</p> <p>17 which shows an increased risk of</p> <p>18 ovarian cancer.</p> <p>19 So you're saying would IARC</p> <p>20 consider that in talc as a</p> <p>21 carcinogen, the asbestos, and I'm</p> <p>22 saying yes, they considered -- in</p> <p>23 your supposition, would</p> <p>24 asbestiform talc be considered a</p>	<p>1 clarify my opinion, because my</p> <p>2 opinion is really, I think,</p> <p>3 clearly what I'm stating.</p> <p>4 I'm saying that asbestos and</p> <p>5 its relationship to ovarian cancer</p> <p>6 has been clearly shown in a few</p> <p>7 very unlikely situations ever to</p> <p>8 happen again. And those are those</p> <p>9 prospective cohort studies.</p> <p>10 I'm saying that IARC,</p> <p>11 extending that outside of those</p> <p>12 situations that they have not</p> <p>13 studied, that's when I'm going to</p> <p>14 go to what are people actually</p> <p>15 using in that bottle.</p> <p>16 And if that's asbestos in</p> <p>17 that bottle, I'm closing this</p> <p>18 book, and I'm opening the talc</p> <p>19 monograph, because that -- all the</p> <p>20 studies that they discuss in that</p> <p>21 talc monograph are these products,</p> <p>22 the Johnson & Johnson products.</p> <p>23 I would be going to the</p> <p>24 case-control studies in my report.</p>
Page 99	Page 101
<p>1 Group 1. I would say according to</p> <p>2 IARC, yes.</p> <p>3 I'm just clarifying to say</p> <p>4 that the whole point of me being</p> <p>5 here is to give an opinion whether</p> <p>6 that supposition that you just</p> <p>7 said, if there is asbestos in Baby</p> <p>8 Powder, Johnson & Johnson's</p> <p>9 product, is that a carcinogen?</p> <p>10 And my answer would be no,</p> <p>11 because I don't see convincing --</p> <p>12 and we're going to go through I'm</p> <p>13 sure all the reasons that I don't</p> <p>14 believe that. But I don't believe</p> <p>15 that it proves that it's a</p> <p>16 carcinogen.</p> <p>17 BY MS. GARBER:</p> <p>18 Q. So then, you disagree with</p> <p>19 IARC that asbestos is not a Group 1</p> <p>20 carcinogen?</p> <p>21 MS. CURRY: Object to form.</p> <p>22 THE WITNESS: No. You're</p> <p>23 oversimplifying my statement. And</p> <p>24 I can't believe it's to really</p>	<p>1 I'd be going to the prospective</p> <p>2 trials in my report.</p> <p>3 I don't understand why we</p> <p>4 would use such an indirect</p> <p>5 comparison, finding something in</p> <p>6 this book to help us figure out</p> <p>7 does that product cause cancer</p> <p>8 when there's been so much research</p> <p>9 using what's in that bottle that</p> <p>10 have results.</p> <p>11 BY MS. GARBER:</p> <p>12 Q. Doctor, my question was just</p> <p>13 way more broad than what -- what you're</p> <p>14 answering.</p> <p>15 Do you agree with IARC that</p> <p>16 asbestos is a Group I carcinogen? I</p> <p>17 didn't mention ovarian cancer. I said do</p> <p>18 you agree with IARC that asbestos is a</p> <p>19 Group I carcinogen?</p> <p>20 MS. CURRY: Object to the</p> <p>21 form.</p> <p>22 THE WITNESS: Yes. In</p> <p>23 certain settings.</p> <p>24 BY MS. GARBER:</p>

Kevin Holcomb, M.D.

Page 102	Page 104
<p>1 Q. And so now if we put a 2 Group I carcinogen in a bottle of talc, 3 then the corollary is that the bottle of 4 talc contains a Group I carcinogen, 5 right? 6 A. That would be true. 7 MS. CURRY: Object to the 8 form. 9 BY MS. GARBER: 10 Q. Thank you. 11 So let's mark your notice of 12 deposition as Exhibit 5. 13 (Document marked for 14 identification as Exhibit 15 Holcomb-5.) 16 BY MS. GARBER: 17 Q. Doctor, we've marked as 18 Exhibit 5 your notice of deposition for 19 today's proceeding. Did you review this 20 before today? 21 A. At some point I did. 22 Q. When did you review it? 23 A. When? 24 Q. Mm-hmm.</p>	<p>1 Q. Your file for this matter is 2 your report? 3 A. Yes. 4 Q. Does it consist of anything 5 else? 6 A. Does my report consist of 7 anything else? 8 Q. No. 9 Is it your testimony, 10 Doctor, that your file in this matter in 11 the MDL consists of your expert report, 12 which is dated February 25, 2019? 13 MS. CURRY: Object to the 14 form. 15 THE WITNESS: Yes. 16 BY MS. GARBER: 17 Q. You don't have any other 18 documents? 19 A. No. 20 Q. And do you have any 21 document -- any scientific literature 22 that consists of your file? 23 MS. CURRY: Object to the 24 form.</p>
Page 103	Page 105
<p>1 A. When it was first produced. 2 Q. And did you review the 3 documents -- 4 MS. GARBER: And I 5 understand you've made objections, 6 Ms. Curry. 7 BY MS. GARBER: 8 Q. But did you review the 9 documents that we asked you to produce? 10 A. Yes. 11 Q. And did you endeavor to 12 comply with that and provide those 13 documents? 14 A. Yes. 15 Q. And have you brought with 16 you Item 3, a copy of your complete files 17 as they relate to the work done 18 concerning talcum powder litigation? 19 MS. CURRY: Object to the 20 form. 21 THE WITNESS: Yes. 22 BY MS. GARBER: 23 Q. And where is that file? 24 A. In my report.</p>	<p>1 THE WITNESS: I don't 2 understand your question. 3 BY MS. GARBER: 4 Q. You've reviewed a number of 5 studies that appear on the reference 6 lists attached to your expert report, 7 correct? 8 A. Correct. 9 Q. Where physically are those 10 literature? 11 A. When you say where 12 physically? 13 Q. Mm-hmm. 14 A. The -- I -- I did most of 15 my -- almost all of it electronically. 16 Q. You didn't receive hard 17 copies of any documents? 18 A. The expert reports I 19 received as a hardcopy. 20 Q. What about with regard to 21 published literature. Did you review 22 any -- did you receive any hard copies of 23 those? 24 A. Not for the MDL.</p>

27 (Pages 102 to 105)

Kevin Holcomb, M.D.

<p style="text-align: right;">Page 106</p> <p>1 Q. You did receive hard copies</p> <p>2 from the Ingham matter, correct?</p> <p>3 A. I did. And I quickly asked</p> <p>4 for electronic copies.</p> <p>5 Q. And did you make any notes</p> <p>6 on those 61 studies that you received in</p> <p>7 connection with Ingham?</p> <p>8 MS. CURRY: Object to the</p> <p>9 form.</p> <p>10 THE WITNESS: No.</p> <p>11 BY MS. GARBER:</p> <p>12 Q. With regard to the</p> <p>13 literature that you reviewed in</p> <p>14 connection with this matter, did you make</p> <p>15 any notes electronically on the data?</p> <p>16 A. No.</p> <p>17 Q. Do you have the data saved</p> <p>18 in a certain file in your computer?</p> <p>19 A. Yes. I imagine it's</p> <p>20 probably somewhere in my download list,</p> <p>21 in my download area.</p> <p>22 Q. Like a DropBox?</p> <p>23 A. No. I'm saying like if it</p> <p>24 was sent electronically, when I</p>	<p style="text-align: right;">Page 108</p> <p>1 that Johnson & Johnson provided you that</p> <p>2 you relied upon in forming your opinions?</p> <p>3 A. No.</p> <p>4 Q. Relating to your opinions as</p> <p>5 set forth in your February 25, 2019,</p> <p>6 litigation report, have you made any</p> <p>7 assumptions?</p> <p>8 A. Please repeat that?</p> <p>9 Q. Sure. Relating to your</p> <p>10 opinions in your expert report in this</p> <p>11 matter, have you made any assumptions?</p> <p>12 MS. CURRY: Object to the</p> <p>13 form.</p> <p>14 THE WITNESS: No.</p> <p>15 BY MS. GARBER:</p> <p>16 Q. Do you assume, in coming to</p> <p>17 your causation opinions regarding talcum</p> <p>18 powder products, that they are free of</p> <p>19 asbestos?</p> <p>20 A. I don't have an opinion on</p> <p>21 it.</p> <p>22 Q. Do you have an opinion as to</p> <p>23 whether Johnson & Johnson products,</p> <p>24 talcum powder products, are free of</p>
<p style="text-align: right;">Page 107</p> <p>1 downloaded it, I would imagine it must be</p> <p>2 in the download part of my computer.</p> <p>3 Q. Have you -- I don't</p> <p>4 understand when you say download of a</p> <p>5 computer, where that would be?</p> <p>6 A. If you get a ZIP file, and</p> <p>7 you open it, it's actually downloading</p> <p>8 stuff to your computer.</p> <p>9 Q. I understand. Okay.</p> <p>10 Have you produced all</p> <p>11 documents that relate to your</p> <p>12 compensation for expert work in this</p> <p>13 matter?</p> <p>14 A. Yes.</p> <p>15 MS. CURRY: Subject to the</p> <p>16 objections.</p> <p>17 BY MS. GARBER:</p> <p>18 Q. And have you produced all</p> <p>19 references that identify facts, or data</p> <p>20 that Johnson & Johnson lawyers provided</p> <p>21 you and you considered in formulating</p> <p>22 your opinions?</p> <p>23 A. Yes.</p> <p>24 Q. Are there any assumptions</p>	<p style="text-align: right;">Page 109</p> <p>1 fibrous talc?</p> <p>2 A. No, I don't have an opinion.</p> <p>3 Q. Do you have an opinion if</p> <p>4 Johnson & Johnson talcum powder products</p> <p>5 contain heavy metals like nickel,</p> <p>6 chromium, cobalt and the like?</p> <p>7 MS. CURRY: Object to the</p> <p>8 form.</p> <p>9 THE WITNESS: I don't have</p> <p>10 an opinion.</p> <p>11 BY MS. GARBER:</p> <p>12 Q. Do you have an opinion</p> <p>13 whether Johnson & Johnson talcum powder</p> <p>14 products contain carcinogenic fragrances?</p> <p>15 MS. CURRY: Object to the</p> <p>16 form.</p> <p>17 THE WITNESS: No, I don't</p> <p>18 have an opinion.</p> <p>19 BY MS. GARBER:</p> <p>20 Q. In the Ingham matter, you</p> <p>21 had no opinion whether Johnson &</p> <p>22 Johnson's talcum powder products</p> <p>23 contained asbestos at any point, right?</p> <p>24 A. I didn't have an opinion,</p>

Kevin Holcomb, M.D.

Page 110	Page 112
<p>1 no.</p> <p>2 Q. Is that still the case?</p> <p>3 A. Still the case.</p> <p>4 (Document marked for</p> <p>5 identification as Exhibit</p> <p>6 Holcomb-6.)</p> <p>7 BY MS. GARBER:</p> <p>8 Q. I'll mark as Exhibit 6 the</p> <p>9 production that was made, I think, the</p> <p>10 25th.</p> <p>11 Doctor, this is a single</p> <p>12 document that is printed on both sides,</p> <p>13 and we'll start with the side that is</p> <p>14 titled "Expert Report of Kevin Holcomb</p> <p>15 For General Or Causation Daubert Hearing,</p> <p>16 Supplemental Materials Received and</p> <p>17 Reviewed By Dr. Kevin Holcomb."</p> <p>18 Doctor, is this the</p> <p>19 supplemental materials that you reviewed</p> <p>20 after you issued your expert report?</p> <p>21 A. Yes.</p> <p>22 Q. Do you need to add any</p> <p>23 further documents to this list to make it</p> <p>24 accurate?</p>	<p>1 Q. And it lists 95 hours of</p> <p>2 expert work?</p> <p>3 A. Yes, it does.</p> <p>4 Q. And at a rate of \$850?</p> <p>5 A. Yes.</p> <p>6 Q. And so you've invoiced</p> <p>7 Johnson & Johnson for \$80,750, right?</p> <p>8 A. That's correct.</p> <p>9 Q. Have you been paid?</p> <p>10 A. No.</p> <p>11 Q. And are there any other</p> <p>12 hours that you intend to invoice Johnson</p> <p>13 & Johnson for?</p> <p>14 A. Yes.</p> <p>15 MS. CURRY: Object to the</p> <p>16 form.</p> <p>17 BY MS. GARBER:</p> <p>18 Q. And how many hours would</p> <p>19 that entail?</p> <p>20 A. Depends on how long we go</p> <p>21 today and the few hours yesterday.</p> <p>22 Q. How many hours yesterday?</p> <p>23 A. Maybe about four.</p> <p>24 Q. And do you intend to bill</p>
Page 111	Page 113
<p>1 A. No.</p> <p>2 Q. And when did you review the</p> <p>3 scientific studies that are listed there?</p> <p>4 A. When you say scientific?</p> <p>5 Q. Aside from the depositions</p> <p>6 and expert reports, when did you review</p> <p>7 each of those papers that are listed</p> <p>8 there, specifically Items 1, 2, 8, 9 and</p> <p>9 10?</p> <p>10 A. That came after reading</p> <p>11 Dr. Saenz's deposition. So I don't know.</p> <p>12 Maybe about a week, week and a half ago.</p> <p>13 Q. Okay. And then if we turn</p> <p>14 the document over, does this reflect an</p> <p>15 invoice issued by you on March 25th,</p> <p>16 2019, to Johnson & Johnson for expert</p> <p>17 services?</p> <p>18 A. Yes, it does.</p> <p>19 Q. And it indicates as to the</p> <p>20 description for literature review,</p> <p>21 drafting of expert report, and</p> <p>22 preparation for deposition; is that</p> <p>23 correct?</p> <p>24 A. That's true.</p>	<p>1 Johnson & Johnson for any work in</p> <p>2 preparation of today's deposition before</p> <p>3 the deposition started today?</p> <p>4 A. No.</p> <p>5 Q. Do you have a different rate</p> <p>6 for your deposition --</p> <p>7 A. No.</p> <p>8 Q. -- as opposed to other work</p> <p>9 that you do?</p> <p>10 A. No.</p> <p>11 Q. How much money were you paid</p> <p>12 with regard to your work in the Ingham</p> <p>13 case?</p> <p>14 A. In total, it was \$100,300.</p> <p>15 Q. And so in connection with</p> <p>16 your work today for Johnson & Johnson in</p> <p>17 connection with talcum powder products,</p> <p>18 ovarian cancer litigation, you have thus</p> <p>19 at least invoiced and/or been paid for</p> <p>20 roughly 183 -- almost \$184,000; is that</p> <p>21 fair?</p> <p>22 MS. CURRY: Object to the</p> <p>23 form.</p> <p>24 THE WITNESS: No.</p>

Kevin Holcomb, M.D.

Page 114	Page 116
<p>1 BY MS. GARBER: 2 Q. How much? 3 A. You said invoiced and been 4 paid? 5 Q. Yeah, so, so you have to 6 date earned \$103,000, correct? 7 A. Correct. 8 Q. And then you've invoiced 9 Johnson & Johnson for \$80,750, correct? 10 A. Correct. 11 Q. Plus the hours that you just 12 mentioned? 13 A. Correct. 14 Q. Is that the totality of the 15 compensation that you have received, or 16 will receive up through today's 17 deposition? 18 A. That is. 19 Q. Thank you. 20 (Document marked for 21 identification as Exhibit 22 Holcomb-7.) 23 BY MS. GARBER: 24 Q. I'm going to mark your</p>	<p>1 with some degree of how strong I thought 2 the studies were, how subject they might 3 be to spurious results. 4 I looked to see if there was 5 consistency. I looked to see if there 6 was a biologic plausibility that involved 7 mainly looking at migration issues. And 8 then in a totality came up with my 9 opinion about the ability of talc to 10 cause ovarian cancer. 11 Q. If we turn to your 12 references which appear beginning at Page 13 25 through 33. And in addition the 14 supplemental references, there are more 15 than the 61 references that you had in 16 connection with the Ingham trial, 17 correct? 18 A. Yes. 19 Q. Did you request any other 20 documents or literature from counsel? 21 MS. CURRY: Object to the 22 form. 23 THE WITNESS: No. 24 BY MS. GARBER:</p>
Page 115	Page 117
<p>1 expert report in the MDL as Exhibit 7. 2 You signed this document on 3 February 25, 2019, correct? 4 A. Correct. 5 Q. And this is your litigation 6 report attendant to the MDL talcum powder 7 products litigation, correct? 8 A. Correct. 9 Q. Have you endeavored to have 10 this litigation report published in any 11 scientific journal? 12 A. No. 13 Q. Can you describe the process 14 you used in developing the opinions 15 contained in this report? 16 A. Yes. I started, again, by 17 reviewing epidemiologic data. I reviewed 18 both case-control and cohort studies. I 19 looked at -- well, I guess my methodology 20 would really be following Bradford Hill's 21 methodology, because in reviewing that 22 data I looked at the strengths of 23 associations. 24 I tried to rate the studies</p>	<p>1 Q. And is it accurate that all 2 of the documents that are listed on your 3 reference lists, which include what's 4 attached to your report and the 5 supplemental, were all provided to you by 6 counsel? 7 MS. CURRY: Object to the 8 form. 9 THE WITNESS: No. Some of 10 these I came up with on my own. I 11 don't remember exactly which ones. 12 But it's not all provided by 13 counsel. 14 BY MS. GARBER: 15 Q. Is there anything you 16 reviewed but did not rely upon in forming 17 your opinions? 18 A. No. 19 Q. Are there any materials that 20 you relied upon in forming your opinions 21 that are not listed in your reference 22 lists that we've reviewed? 23 MS. CURRY: Object to the 24 form.</p>

30 (Pages 114 to 117)

Kevin Holcomb, M.D.

<p style="text-align: right;">Page 118</p> <p>1 THE WITNESS: Other than 2 what I've already told you that I 3 came across in expert reports. 4 BY MS. GARBER: 5 Q. And in drafting your expert 6 report, you have not made any notes; is 7 that correct? 8 A. If you mean written, no. I 9 would -- as the manuscript was being 10 produced, I would make points. But it 11 all became incorporated in the end into a 12 final product. 13 Q. What was the process by 14 which you developed your report? Did you 15 read a study and then make some notes or 16 mental notes, or write? Tell me the 17 process by which you -- 18 MS. CURRY: Object to the 19 form. 20 THE WITNESS: I typically 21 worked with two monitors. And one 22 I'm writing the manuscript. The 23 other one, I'm bringing up papers. 24 BY MS. GARBER:</p>	<p style="text-align: right;">Page 120</p> <p>1 Q. What were your -- what was 2 your search engine? 3 A. PubMed as you mentioned. 4 Sometimes Google. 5 Q. And what were your search 6 terms? 7 A. Ovarian cancer, talc, 8 perineal talc and ovarian cancer, body 9 powder and ovarian cancer. It depended 10 what I was looking for. 11 There was some points I'm 12 making in my expert report where I'm 13 using analogies. And so I was looking at 14 HPV and cervical cancer or herpes simplex 15 virus and cervical cancer. And so it -- 16 it depended on what I was -- what I was 17 looking at at the moment. 18 Q. What did you do, Google 19 searches? 20 A. I'm guilty of using Google 21 from now and then to start a search. 22 It's sometimes faster. It will bring up 23 PubMed articles. 24 Q. Did -- have you read, since</p>
<p style="text-align: right;">Page 119</p> <p>1 Q. Okay. So there's no notes 2 that you made before you started to sit 3 down and write your expert report; is 4 that correct? 5 MS. CURRY: Object to the 6 form. 7 THE WITNESS: No. 8 BY MS. GARBER: 9 Q. It's not correct? 10 A. There are no notes. 11 Q. There are -- thank you. 12 Did you read every word of 13 the documents listed in your reference 14 list? 15 A. Yes. 16 Q. Did you -- when you said you 17 obtained some of the references, is that 18 limited to reviewing exhibits from expert 19 reports or depositions? 20 A. No. 21 Q. Did you conduct any 22 searches, say, Medline searches or PubMed 23 searches? 24 A. I did.</p>	<p style="text-align: right;">Page 121</p> <p>1 the production of your supplemental 2 reference list, have you read any other 3 expert reports or depositions or other 4 studies? 5 A. Since? 6 Q. Since the production of your 7 supplemental expert report which was 8 marked as Exhibit 6. 9 MS. CURRY: Object to the 10 form. You mean supplemental 11 materials received list? 12 MS. GARBER: Yes. 13 THE WITNESS: Only -- let's 14 see. Yes, there's one other -- 15 one other paper, and that was a 16 migration paper. But I believe it 17 just came out. It was -- 18 BY MS. GARBER: 19 Q. What's the title? 20 A. I don't remember. 21 Q. Or the author? 22 A. It was -- I don't know who 23 is the first author. I know -- 24 Q. Can you give me any authors?</p>

Kevin Holcomb, M.D.

Page 122	Page 124
<p>1 A. Cramer was -- was involved. 2 I don't remember the first author though. 3 Q. What was the nature of that 4 paper? 5 A. It was -- 6 MS. CURRY: Object to the 7 form. 8 THE WITNESS: It was a paper 9 looking at an attempt to try to 10 differentiate contamination from 11 actual migration of talc 12 particles. 13 BY MS. GARBER: 14 Q. What did you glean from that 15 paper, Doctor? 16 MS. CURRY: Object to the 17 form. 18 THE WITNESS: The biggest 19 thing that I gleaned was that 20 contamination is -- it's probably 21 even more widespread than I 22 realized. And I appreciated the 23 effort to try to distinguish 24 between the two, but I wasn't</p>	<p>1 expert reports or depositions after the 2 supplemental reference list? 3 A. No. 4 Q. And it is accurate that 5 prior to signing your expert report on 6 February 25, 2019, you had not read the 7 recent Saed 2019 paper with regard to a 8 molecular basis supporting the 9 association of talcum powder use with 10 increased risk of ovarian cancer, right? 11 MS. CURRY: Object to the 12 form. 13 THE WITNESS: I'm sorry, can 14 you repeat the question again? 15 Prior to -- 16 BY MS. GARBER: 17 Q. Sure. 18 Prior to signing your expert 19 report on February 25, 2019, you had not 20 read Dr. Saed's 2019 publication, 21 correct? 22 A. That's true. 23 MS. CURRY: Same objection. 24 Sorry.</p>
Page 123	Page 125
<p>1 convinced that you can 2 necessarily. 3 BY MS. GARBER: 4 Q. Did the authors there 5 attempt to distinguish surface 6 contamination from talc that was deeply 7 embedded in the tissue? 8 A. Well, they were only looking 9 at lymph nodes from my memory. So they 10 were trying to distinguish between 11 particles on the surface and particles 12 that are in, deeper inside the lymph node 13 itself, yes. 14 Q. Does that paper provide a 15 basis for any of your expert opinions 16 today? 17 A. No. 18 Q. You did not rely upon -- you 19 do not rely upon the Cramer -- we'll call 20 it Cramer contamination paper -- for 21 purposes of your expert opinions; is that 22 fair? 23 A. That's fair. 24 Q. Did you read any other</p>	<p>1 BY MS. GARBER: 2 Q. Prior to signing your expert 3 report on February 25, 2019, likewise you 4 had not read Dr. Saed's abstract with 5 regard to talc and ROS induction, 6 correct? 7 A. That's true. 8 Q. You indicate at Page 20 -- 9 MS. CURRY: Do you need a 10 break? 11 THE WITNESS: Well, I wasn't 12 sure if I -- it looks like we're 13 going to be close to lunch so... 14 We'll be planning on 15 breaking around 12 or -- 16 MS. CURRY: Sorry. I 17 thought he had a message from the 18 hospital, so I wanted to make sure 19 if he needs to take a break. 20 We've been going over an hour, 21 Susan, so whenever is a good time 22 for you. 23 MS. GARBER: You want to 24 take a break? Whenever you</p>

32 (Pages 122 to 125)

Kevin Holcomb, M.D.

Page 126	Page 128
<p>1 guys --</p> <p>2 THE WITNESS: I'm fine for a</p> <p>3 break.</p> <p>4 MS. GARBER: You want to</p> <p>5 take a break?</p> <p>6 THE WITNESS: Yeah, I'd</p> <p>7 appreciate it.</p> <p>8 MS. GARBER: Okay.</p> <p>9 THE VIDEOGRAPHER: Please</p> <p>10 remove your microphones. The time</p> <p>11 is 11:28 a.m. Going off the</p> <p>12 record.</p> <p>13 (Short break.)</p> <p>14 THE VIDEOGRAPHER: Okay. We</p> <p>15 are back on the record. The time</p> <p>16 is 11:42 a.m.</p> <p>17 BY MS. GARBER:</p> <p>18 Q. Doctor, you state at Page 22</p> <p>19 of your report that plaintiffs' expert</p> <p>20 gynecologic oncologist conducted a</p> <p>21 selective review of the study on biologic</p> <p>22 mechanism.</p> <p>23 What studies do you</p> <p>24 contend --</p>	<p>1 they do acknowledge that, but they</p> <p>2 don't -- they don't describe it.</p> <p>3 They just say considered limited</p> <p>4 evidence to the contrary and find</p> <p>5 it non-persuasive.</p> <p>6 My review of the literature</p> <p>7 on this topic, I was looking for</p> <p>8 some studies showing that you</p> <p>9 could dust the human vulva with</p> <p>10 talc and show that those particles</p> <p>11 can make it to the ovary, and I</p> <p>12 couldn't find a single study in</p> <p>13 that situation.</p> <p>14 You could place particles in</p> <p>15 the vagina. You can give a</p> <p>16 patient oxytocin. You can do</p> <p>17 some -- you know, different --</p> <p>18 different than the majority of the</p> <p>19 use of these products.</p> <p>20 And so I -- I came to the</p> <p>21 conclusion that their -- their</p> <p>22 approach was conclusion driven,</p> <p>23 just because it seemed to me, if</p> <p>24 you've never seen a study that</p>
Page 127	Page 129
<p>1 A. Could you -- could you</p> <p>2 point -- I'm not sure where you're</p> <p>3 reading from.</p> <p>4 Q. From Page 22 of your expert</p> <p>5 report.</p> <p>6 A. Right, where -- I'm just</p> <p>7 looking where on the page it says this.</p> <p>8 Q. At the first full paragraph.</p> <p>9 MS. CURRY: I'm not seeing</p> <p>10 it there either.</p> <p>11 THE WITNESS: I see where</p> <p>12 you're saying.</p> <p>13 You're saying, "Such</p> <p>14 selective review of studies is</p> <p>15 clearly conclusion driven."</p> <p>16 Q. Yeah, okay. So what -- what</p> <p>17 studies do you believe were omitted from</p> <p>18 the expert -- from the plaintiffs'</p> <p>19 experts?</p> <p>20 MS. CURRY: Object to the</p> <p>21 form.</p> <p>22 THE WITNESS: There's animal</p> <p>23 studies showing no ascension of --</p> <p>24 of particles and -- and they --</p>	<p>1 shows it's possible, and then you</p> <p>2 just say well, the -- the studies</p> <p>3 that I did say that it doesn't</p> <p>4 happen in an animal model, I</p> <p>5 don't -- I'm not persuaded by</p> <p>6 that.</p> <p>7 BY MS. GARBER:</p> <p>8 Q. What animal studies did you</p> <p>9 review with regard to migration?</p> <p>10 A. Yeah, I'd have to look back</p> <p>11 and see was -- whether it was the -- the</p> <p>12 rat model or the pig model. But there</p> <p>13 were definitely animal model studies.</p> <p>14 Let me just show you. It's</p> <p>15 in the -- in the talc monograph, if you</p> <p>16 want me to, I can go back through and --</p> <p>17 and find the citations of --</p> <p>18 Q. That's okay, Doctor.</p> <p>19 I want to know what animal</p> <p>20 studies you think plaintiffs' experts</p> <p>21 should have looked at in connection with</p> <p>22 migration.</p> <p>23 A. Well, it's exactly my point.</p> <p>24 What I'm saying is the study they should</p>

Kevin Holcomb, M.D.

Page 130	Page 132
<p>1 look at would be the study where someone</p> <p>2 dusted the human perineum with talc and</p> <p>3 showed that it was able to reach the</p> <p>4 ovary, and that doesn't exist. So that</p> <p>5 would be the best thing to look at.</p> <p>6 The studies that I mentioned</p> <p>7 to you, which I can go back to the talc</p> <p>8 monograph and find, I don't remember if</p> <p>9 it was Sprague rats or if it was actually</p> <p>10 pigs or guinea pigs. There was a couple</p> <p>11 of animal models where they were not able</p> <p>12 to show migration from the vagina, not --</p> <p>13 much less the perineum.</p> <p>14 Q. It's your testimony that</p> <p>15 plaintiffs' experts didn't look at a</p> <p>16 human study that dusted the perineum with</p> <p>17 talc and it was shown to migrate to the</p> <p>18 ovaries, and you're critical of that even</p> <p>19 though such a study does not exist?</p> <p>20 MS. CURRY: Object to the</p> <p>21 form.</p> <p>22 THE WITNESS: You know, I</p> <p>23 guess what you can be critical of,</p> <p>24 and I'd have to admit to that is,</p>	<p>1 THE WITNESS: I'm not sure</p> <p>2 what you mean by comprehensive. I</p> <p>3 will tell you that the studies</p> <p>4 that I do cite, for example a</p> <p>5 study like Heller, where there's</p> <p>6 no correlation between the</p> <p>7 presence of talc in someone's</p> <p>8 ovaries and the reported use of</p> <p>9 talc, which I'm sure the</p> <p>10 plaintiffs' experts have seen,</p> <p>11 should give them reason to pause</p> <p>12 if they've never been able to show</p> <p>13 it in a human model that it can</p> <p>14 happen.</p> <p>15 And then you see studies</p> <p>16 like that that say there's no</p> <p>17 correlation between reported</p> <p>18 history and the presence of talc</p> <p>19 in the ovaries, that it should</p> <p>20 make you -- it should make you</p> <p>21 wonder.</p> <p>22 And I wouldn't be so</p> <p>23 dismissive of the studies that are</p> <p>24 to the contrary. I mean, they're</p>
Page 131	Page 133
<p>1 I'm saying such selective</p> <p>2 review -- and I guess that's not</p> <p>3 what's being selective here.</p> <p>4 What's being selective is what you</p> <p>5 consider persuasive or not.</p> <p>6 It's not the review. It's</p> <p>7 the absence of such a study. And</p> <p>8 then not finding the studies on</p> <p>9 animal models that don't show</p> <p>10 ascension as not being persuasive.</p> <p>11 BY MS. GARBER:</p> <p>12 Q. Doctor, I reviewed your</p> <p>13 reference list, and I can find about</p> <p>14 three studies with regard to the issue of</p> <p>15 migration. And my question to you is,</p> <p>16 did you do a comprehensive review of the</p> <p>17 literature with regard to the ability of</p> <p>18 talc to migrate from the genitals to the</p> <p>19 perineum --</p> <p>20 MS. CURRY: Objection.</p> <p>21 BY MS. GARBER:</p> <p>22 Q. -- or to the ovaries?</p> <p>23 MS. CURRY: Object to the</p> <p>24 form.</p>	<p>1 mentioning, "Reviewed the small</p> <p>2 body of literature suggesting</p> <p>3 migration of particles does not</p> <p>4 occur." So they're admitting that</p> <p>5 there is a body of literature that</p> <p>6 shows that it doesn't occur.</p> <p>7 BY MS. GARBER:</p> <p>8 Q. Doctor --</p> <p>9 A. You can go --</p> <p>10 Q. Doctor, if you can --</p> <p>11 MS. CURRY: Are you finished</p> <p>12 with your response?</p> <p>13 THE WITNESS: Yeah.</p> <p>14 BY MS. GARBER:</p> <p>15 Q. Can you turn to Page --</p> <p>16 A. Can I finish my answer?</p> <p>17 So --</p> <p>18 Q. You can finish.</p> <p>19 A. Thank you.</p> <p>20 So the statement that says,</p> <p>21 "I've reviewed the small body of</p> <p>22 literature suggesting that migration of</p> <p>23 particles does not occur," they're</p> <p>24 describing that body of literature as</p>

Kevin Holcomb, M.D.

Page 134	Page 136
<p>1 small. And I'm saying that there is no</p> <p>2 body of literature showing that perineal</p> <p>3 dusting of talc gets to the ovaries.</p> <p>4 So you're comparing small to</p> <p>5 none, but you find the small</p> <p>6 non-persuasive.</p> <p>7 Q. Doctor, if you can turn to</p> <p>8 Page 16 of your expert report. There is</p> <p>9 a section on Page 16 titled "Migration of</p> <p>10 Talc Particles," correct?</p> <p>11 A. Yes.</p> <p>12 Q. And you mention the Wehner</p> <p>13 paper, correct?</p> <p>14 A. Yes.</p> <p>15 Q. And do you know what -- was</p> <p>16 that an animal study or human study?</p> <p>17 A. That was animals.</p> <p>18 Q. All right. And then you</p> <p>19 mentioned the Heller study. Was that a</p> <p>20 talc migration study? In other words,</p> <p>21 was talc placed at the genitals and</p> <p>22 looked to see if it travels?</p> <p>23 A. No.</p> <p>24 Q. Okay. And then you also</p>	<p>1 you're going to develop a model to say --</p> <p>2 Q. Doctor, sorry, I'm just</p> <p>3 going to cut you off.</p> <p>4 A. Sure.</p> <p>5 Q. My question was did you --</p> <p>6 it was just a really simple question.</p> <p>7 Did you look at any other human studies.</p> <p>8 And the answer was yes?</p> <p>9 A. Yes.</p> <p>10 Q. And then you mentioned one</p> <p>11 study; is that right? Were there any</p> <p>12 other studies?</p> <p>13 MS. CURRY: Object to the</p> <p>14 form.</p> <p>15 THE WITNESS: I would have</p> <p>16 to go back and remind myself of</p> <p>17 how many, but it was more than</p> <p>18 one.</p> <p>19 BY MS. GARBER:</p> <p>20 Q. Do you have any other</p> <p>21 criticisms of plaintiffs' gynecologic</p> <p>22 oncologists and the claim that they</p> <p>23 selectively reviewed studies? Any other</p> <p>24 criticisms as to the body of literature?</p>
Page 135	Page 137
<p>1 mentioned the Cramer study, right, the</p> <p>2 2007 study?</p> <p>3 A. Yes.</p> <p>4 2007, you said?</p> <p>5 Q. Yes.</p> <p>6 A. Oh, yes, yes.</p> <p>7 Q. And then if we turn the page</p> <p>8 over, you also mention the Gertig study;</p> <p>9 is that right?</p> <p>10 A. Yes.</p> <p>11 Q. And then you mention the</p> <p>12 Terry study?</p> <p>13 A. Right.</p> <p>14 Q. Doctor, did you look at any</p> <p>15 of the human studies where particulate</p> <p>16 was placed at the genitals or in the</p> <p>17 genitals and the ability to migrate?</p> <p>18 A. What particular particulate</p> <p>19 are you talking about?</p> <p>20 Q. Any particulate.</p> <p>21 A. Yes. And I saw in expert --</p> <p>22 for example, in Dr. Birrer's report, I</p> <p>23 believe he discusses a study of carbon.</p> <p>24 But I think it's really important if</p>	<p>1 A. I do.</p> <p>2 MS. CURRY: Object to the</p> <p>3 form.</p> <p>4 THE WITNESS: I do. I</p> <p>5 looked at the literature in</p> <p>6 totality. So if you just restrict</p> <p>7 to the epidemiologic data, I</p> <p>8 looked at the case-control</p> <p>9 studies. I spent a fair amount of</p> <p>10 time going through those, looking</p> <p>11 for consistency and things like</p> <p>12 that.</p> <p>13 And then I looked at the</p> <p>14 cohort studies, which as you see</p> <p>15 in my report I explain why they</p> <p>16 may -- they are generally</p> <p>17 considered to be less prone to</p> <p>18 bias.</p> <p>19 And then I read</p> <p>20 Dr. Clarke-Pearson's report where</p> <p>21 he almost -- I don't even think he</p> <p>22 mentioned the cohort studies,</p> <p>23 which to me was an important thing</p> <p>24 that you'd have to explain away if</p>

35 (Pages 134 to 137)

Kevin Holcomb, M.D.

Page 138	Page 140
<p>1 you really believe that talc 2 causes ovarian cancer. 3 I did -- as I mention, I 4 think they take as a given that 5 talc can migrate. And they're not 6 alone in this. I don't -- I don't 7 think that they're alone in doing 8 that. I read a number of papers 9 that in the introduction will make 10 statements like, "We all know talc 11 can get to the ovaries," and then 12 offer no citation for it. 13 And so I take issue with 14 that as well. 15 BY MS. GARBER: 16 Q. Doctor, I didn't ask you for 17 a full list of your opinions. 18 A. I thought you did. 19 Q. I asked you -- 20 A. You asked me what areas do I 21 disagree with them. 22 Q. Okay. And you mentioned -- 23 MS. CURRY: Please let him 24 finish his response. You've cut</p>	<p>1 THE WITNESS: That's 2 correct. 3 BY MS. GARBER: 4 Q. And those papers relied on 5 plaintiffs' experts in support of their 6 biologically plausible mechanism of 7 carcinogenicity, true? 8 A. Yes, that's true. 9 Q. And in Page 23 of your 10 report you state, "I understand that 11 there are a number of irregularities in 12 Dr. Saed's work and his lab notes." 13 What is your source of that 14 statement? 15 A. Dr. Birrer's expert report. 16 Q. When did you read 17 Dr. Birrer's expert report? 18 A. I'm trying to think. 19 Probably about maybe two weeks ago. 20 Can you tell me what you're 21 referring to though? 22 Your -- your statement. You 23 said you -- I made a -- a referral to 24 something about Dr. Saed, but you didn't</p>
Page 139	Page 141
<p>1 him off twice now. 2 MS. GARBER: That's because 3 he's talking in very large 4 paragraphs, and we're never going 5 to get anywhere if I don't. 6 MS. CURRY: If you ask these 7 broad, open-ended questions, he's 8 entitled to respond to it. 9 MS. GARBER: All right. 10 I'll ask a different question. 11 BY MS. GARBER: 12 Q. Doctor, did you review the 13 Buz'Zard 2007, Shukla 2009 papers? 14 A. Only with regard to the 15 expert reports. 16 Q. They're not on your 17 reference list, are they? 18 A. No. 19 Q. And you did not review the 20 Saed 2019 prior to signing your expert 21 report. We've already established that, 22 right? 23 MS. CURRY: Object to the 24 form.</p>	<p>1 tell me where to find it. 2 Q. I just asked you generally, 3 Doctor. 4 You -- you made mention 5 that -- that his work and lab notes -- 6 A. I'm just asking where you're 7 reading from, if you can -- 8 Q. At Page 23, Doctor. 9 A. 23. Thank you. 10 Q. So what's your source of 11 that statement? 12 A. Hold on one second. 13 Q. If you don't know, we'll 14 move on. 15 MS. CURRY: Just give him a 16 second to look at where you're 17 reading from. 18 THE WITNESS: I just want to 19 get to -- yeah. 20 BY MS. GARBER: 21 Q. It's at the top of 23. 22 A. I don't remember exactly. 23 Q. All right. Did you -- I -- 24 I noted that his lab notebooks were not</p>

Kevin Holcomb, M.D.

<p style="text-align: right;">Page 142</p> <p>1 on his reference list. You didn't look 2 at those, did you? 3 MS. CURRY: Object to the 4 form. 5 THE WITNESS: No. 6 BY MS. GARBER: 7 Q. You haven't looked at all of 8 his work relating to talc and mechanism 9 of carcinogenicity, right? 10 A. No. 11 Q. And with regard to your 12 reference list, you haven't reviewed 13 Health Canada's draft screening 14 assessment with regard to talc dated 15 December of 2018, correct? 16 MS. CURRY: Object to the 17 form. 18 THE WITNESS: I did. 19 BY MS. GARBER: 20 Q. Sorry? 21 A. I did. 22 Q. You did review it? 23 A. It's one of Dr. Saenz's 24 exhibits.</p>	<p style="text-align: right;">Page 144</p> <p>1 Q. Are you planning to provide 2 any comment? 3 A. What I reviewed was a draft. 4 So I'm not sure what Health Canada is 5 going to finally decide to publish. So 6 no, I didn't -- I didn't -- 7 Q. Do -- 8 MS. GARBER: Motion to 9 strike as nonresponsive. 10 BY MS. GARBER: 11 Q. Doctor, I asked you, are you 12 planning to provide any comment to Health 13 Canada? 14 A. I'm saying perhaps I would 15 if I saw a final product that I thought 16 was really egregious, but I've only 17 reviewed a draft and so I -- I can't say 18 whether I would or not. 19 Q. Doctor, do you understand 20 that Health Canada has asked for public 21 comment? 22 A. I didn't -- no, I wasn't 23 aware of the process. 24 Q. Okay. Have you ever been</p>
<p style="text-align: right;">Page 143</p> <p>1 Q. Okay. And it's not listed 2 on your reference list, correct? 3 MS. CURRY: Object to the 4 form. 5 THE WITNESS: I'd have to 6 look through the reference list -- 7 no, it was something that I 8 reviewed as part of Dr. Saenz's 9 exhibits. 10 BY MS. GARBER: 11 Q. So you have reviewed Health 12 Canada's December 2018 draft report? 13 A. It's part of Dr. -- it's 14 part of Dr. Saenz's exhibits and I have 15 reviewed it. 16 Q. When did you review that? 17 A. Maybe about a week ago. 18 Q. Okay. Have you read any 19 comment letters or reports issued in 20 response to the Health Canada DSAR? 21 A. No. 22 Q. Have you been asked to 23 provide any comment to Health Canada? 24 A. No.</p>	<p style="text-align: right;">Page 145</p> <p>1 asked to testify at any United States or 2 state government proceedings with regard 3 to talcum powder products? 4 A. No. 5 Q. And you are not conducting 6 any research, experimental research in 7 any capacity concerning talcum powder 8 products and ovarian cancer, right? 9 A. No. 10 Q. Are you planning to? 11 A. No. 12 Q. Have you ever applied for a 13 grant or monies to conduct a research on 14 talcum powder products and ovarian 15 cancer? 16 A. No. 17 Q. Have you read the Taher 2018 18 meta-analysis? 19 A. I have. 20 Q. Yes? 21 A. Yes. 22 Q. When did you read that? 23 A. Same day I read the Health 24 Canada assessment.</p>

37 (Pages 142 to 145)

Kevin Holcomb, M.D.

<p style="text-align: right;">Page 146</p> <p>1 Q. And that was not on any of</p> <p>2 your -- the Taher 2018 meta-analysis was</p> <p>3 not listed on any of your reference</p> <p>4 lists, correct?</p> <p>5 A. It is --</p> <p>6 MS. CURRY: Object to the</p> <p>7 form.</p> <p>8 THE WITNESS: It's also part</p> <p>9 of the exhibits for Dr. Saenz.</p> <p>10 BY MS. GARBER:</p> <p>11 Q. Could you go back to</p> <p>12 Exhibit 6, please.</p> <p>13 Doctor, you understand that</p> <p>14 your reference lists provide me an</p> <p>15 opportunity to know what literature you</p> <p>16 have reviewed and relied on attendant to</p> <p>17 your expert opinions, correct?</p> <p>18 A. That's correct.</p> <p>19 Q. And if you look at Item 5 of</p> <p>20 Exhibit 6 which is your supplemental</p> <p>21 materials?</p> <p>22 A. Yes.</p> <p>23 Q. Could you read Number 5 for</p> <p>24 me, please?</p>	<p style="text-align: right;">Page 148</p> <p>1 A. No, I have not.</p> <p>2 Q. And your expert report</p> <p>3 contains Table 1, correct?</p> <p>4 A. Yes.</p> <p>5 Q. And what is the nature of</p> <p>6 Table 1?</p> <p>7 A. Table 1 --</p> <p>8 MS. CURRY: Table 1 in the</p> <p>9 copy that you marked is actually</p> <p>10 cut off.</p> <p>11 Do you have a full version</p> <p>12 of it?</p> <p>13 MS. GARBER: I do. It's --</p> <p>14 it's buried. But I'm going to</p> <p>15 mark it, so...</p> <p>16 BY MS. GARBER:</p> <p>17 Q. Are you able to tell me what</p> <p>18 Table 1 contains?</p> <p>19 A. Yes.</p> <p>20 Q. And what it is?</p> <p>21 A. Table 1 is a list of</p> <p>22 case-control studies that I reviewed in</p> <p>23 regard to this matter.</p> <p>24 Q. Why did you create this</p>
<p style="text-align: right;">Page 147</p> <p>1 A. It says, "Expert report of</p> <p>2 Cheryl Saenz, M.D., February 25, 2019."</p> <p>3 Q. It doesn't say exhibits,</p> <p>4 does it?</p> <p>5 MS. CURRY: Object to the</p> <p>6 form. Number 3 discusses the</p> <p>7 deposition.</p> <p>8 BY MS. GARBER:</p> <p>9 Q. Is that what it says,</p> <p>10 Doctor? Does it say exhibits there, sir?</p> <p>11 MS. CURRY: Object to the</p> <p>12 form.</p> <p>13 THE WITNESS: It clearly</p> <p>14 doesn't say exhibits. Number 3 is</p> <p>15 where it says exhibits, so I'm not</p> <p>16 sure why you're having me read all</p> <p>17 of 5, when it clearly says on</p> <p>18 Number 3, "Deposition of Cheryl</p> <p>19 Saenz, M.D., and exhibits,</p> <p>20 March 13, 2019."</p> <p>21 BY MS. GARBER:</p> <p>22 Q. Okay. Doctor, have you</p> <p>23 spoken with any of the Taher study</p> <p>24 authors?</p>	<p style="text-align: right;">Page 149</p> <p>1 list?</p> <p>2 A. One, I wanted to show that I</p> <p>3 performed a comprehensive review. But I</p> <p>4 guess largely what I saw mentions over</p> <p>5 and over again by plaintiffs' experts and</p> <p>6 sometimes in other papers, the statement</p> <p>7 that the epidemiologic data consistently</p> <p>8 shows an increased risk of -- of ovarian</p> <p>9 cancer with talc exposure. And I think</p> <p>10 most people already know that that's only</p> <p>11 with case-control studies and none of the</p> <p>12 cohort studies if you include Gates and</p> <p>13 then update to Gertig.</p> <p>14 So then I wanted to look at</p> <p>15 the case-control studies. And to see</p> <p>16 could somebody use that term</p> <p>17 consistently, maybe loosely, and what I</p> <p>18 consider consistent and they consider</p> <p>19 consistent different.</p> <p>20 And so I looked through this</p> <p>21 list of case-control studies. I looked</p> <p>22 at those that showed a positive</p> <p>23 association and had a 95 percent</p> <p>24 confidence interval that would suggest it</p>

Kevin Holcomb, M.D.

Page 150	Page 152
<p>1 was statistically significant. And I 2 wanted to see what percentage of them, 3 that were not duplicates of the same 4 dataset actually showed this association. 5 And so my -- my review of 6 this list of case-control studies was 7 that -- I don't -- it came out to be 8 about 50/50 with a positive association. 9 Because I wanted to find out, would -- 10 would anybody call, you know, a 50/50 11 chance consistent. 12 Q. So you created Table 1 to 13 show or to support your claim that the 14 case-control studies were inconsistent 15 based on statistical significance. 16 Is that fair, Doctor? 17 MS. CURRY: Object to the 18 form. 19 THE WITNESS: That's fair. 20 BY MS. GARBER: 21 Q. Okay. Exhibit A at the back 22 of your expert report is your CV, right? 23 A. Yes. 24 Q. When did you last update it?</p>	<p>1 its levels were higher in women who 2 specifically had clear cell carcinoma. 3 Q. Do any of the publications 4 that do not appear on your reference list 5 concern any of the issues that you deem 6 relevant in this case? 7 MS. CURRY: Object to the 8 form. 9 THE WITNESS: Please repeat 10 that. 11 BY MS. GARBER: 12 Q. Do any of the publications 13 that do not appear on your CV, 14 bibliography, do any -- are any of those 15 relevant as you deem them to the issues 16 in this case? 17 A. I just wanted to clarify. 18 You're asking if any of the papers that 19 I'm a co-author or author on relevant to 20 this topic? 21 Q. That do not appear on your 22 CV? 23 A. That do not appear on my CV? 24 Q. Yes. The ones that you say</p>
Page 151	Page 153
<p>1 A. I believe this is the most 2 recent copy. Let's see. 3 Let's see. This last paper 4 is from January 2019, probably like 5 February or maybe early March. 6 Q. Do you need to make any 7 amendments to make it accurate today? 8 A. I have a few more accepted 9 publications, but they are not up on 10 PubMed, so I don't think so. 11 Q. Do they concern ovarian 12 cancer? 13 A. No. Oh, hold on. I'm 14 sorry. 15 Yes. 16 Q. In what capacity? 17 A. There's one study, which 18 deals with early detection of ovarian 19 cancer where we looked at vaginal fluid 20 as a potential biomarker for women who 21 have an adnexa mass to pick up whether 22 they have ovarian cancer. And we looked 23 at a chemical called LPA, 24 lysophosphatidic acid, and showed that</p>	<p>1 that are not published yet. 2 A. Oh, no. 3 Q. No, they do not concern -- 4 A. No, they do not concern talc 5 and ovarian cancer. 6 Q. Do you consider yourself a 7 research cancer biologist? 8 MS. CURRY: Object to the 9 form. 10 THE WITNESS: No, I would 11 consider someone who does mainly 12 basic science research a 13 biologist. 14 BY MS. GARBER: 15 Q. You don't conduct in vitro 16 studies as part of your practice, right? 17 A. If you see my CV, you'll see 18 some studies that involve in vitro 19 studies. So I collaborate with Ph.Ds. 20 So I'm part of a research team that does 21 perform -- 22 Q. But you don't do the bench 23 work, do you? 24 A. I'm not doing the bench</p>

39 (Pages 150 to 153)

Kevin Holcomb, M.D.

Page 154	Page 156
<p>1 work, no.</p> <p>2 Q. All right. And you don't</p> <p>3 have any degrees in epidemiology, right?</p> <p>4 A. No.</p> <p>5 Q. Did you review any internal</p> <p>6 documents of defendants in this case that</p> <p>7 were produced attendant to this</p> <p>8 litigation?</p> <p>9 A. No, I have not.</p> <p>10 Q. And do you understand that</p> <p>11 United States Senate seeking internal</p> <p>12 company documents relevant to their</p> <p>13 investigation as to whether Johnson &</p> <p>14 Johnson has misrepresented the truth</p> <p>15 about asbestos content in their talcum</p> <p>16 powder products?</p> <p>17 A. I am aware.</p> <p>18 Q. You understand that the</p> <p>19 public, which includes scientists, are</p> <p>20 not normally allowed to review internal</p> <p>21 company documents because manufacturers</p> <p>22 like Johnson & Johnson mark them</p> <p>23 confidential and disclosure can result in</p> <p>24 violation of a protective order? Do you</p>	<p>1 their opinions were based on informed</p> <p>2 scientific medical judgment?</p> <p>3 MS. CURRY: Object to the</p> <p>4 form.</p> <p>5 THE WITNESS: No.</p> <p>6 BY MS. GARBER:</p> <p>7 Q. You disagree with that?</p> <p>8 A. No.</p> <p>9 Q. Pardon?</p> <p>10 A. I disagree with it.</p> <p>11 Q. Which experts -- and I don't</p> <p>12 need to know why. Which experts do you</p> <p>13 think of uninformed scientific opinions?</p> <p>14 MS. CURRY: Object to the</p> <p>15 form.</p> <p>16 THE WITNESS: I would say</p> <p>17 Dr. Clarke-Pearson, Dr. Judith</p> <p>18 Wolf, Ellen Blair Smith.</p> <p>19 BY MS. GARBER:</p> <p>20 Q. Any others?</p> <p>21 A. No, I would restrict it to</p> <p>22 that.</p> <p>23 Q. Okay. And your criticisms</p> <p>24 of those particular doctors as referenced</p>
Page 155	Page 157
<p>1 understand that?</p> <p>2 MS. CURRY: Object to the</p> <p>3 form.</p> <p>4 THE WITNESS: No, I --</p> <p>5 BY MS. GARBER:</p> <p>6 Q. Do you understand how that</p> <p>7 works?</p> <p>8 A. No, I didn't know that.</p> <p>9 Q. You do?</p> <p>10 A. I don't know that.</p> <p>11 Q. Okay. Do I now have a full</p> <p>12 list of the documents that you considered</p> <p>13 in formulating your opinions as</p> <p>14 referenced in your expert report and</p> <p>15 supplemental materials?</p> <p>16 A. Yes.</p> <p>17 Q. Do you understand, Doctor,</p> <p>18 that I'm entitled to know the literature</p> <p>19 that you considered and the foundation</p> <p>20 for your opinions?</p> <p>21 A. Yes.</p> <p>22 Q. And while you don't agree</p> <p>23 with plaintiffs' causation opinions that</p> <p>24 you reviewed, you do acknowledge that</p>	<p>1 in your expert report, does that consist</p> <p>2 of -- strike that.</p> <p>3 The opinions with regard to</p> <p>4 plaintiffs' experts, Dr. Clarke-Pearson,</p> <p>5 Wolf, and Blair Smith, your criticisms of</p> <p>6 those experts are contained within your</p> <p>7 expert report; is that fair?</p> <p>8 A. That's fair.</p> <p>9 Q. Do you agree that experts</p> <p>10 must use scientific judgment when</p> <p>11 assessing the literature for causality?</p> <p>12 A. Yes, I do.</p> <p>13 Q. And in assessing the</p> <p>14 literature, one person's scientific</p> <p>15 judgment may be different than another</p> <p>16 person's scientific judgment?</p> <p>17 MS. CURRY: Object to the</p> <p>18 form.</p> <p>19 THE WITNESS: I believe</p> <p>20 scientific judgment has a role,</p> <p>21 but I believe that there are</p> <p>22 things that are right and wrong as</p> <p>23 well. And I gave you an example</p> <p>24 of one of them, which was it's</p>

40 (Pages 154 to 157)

Kevin Holcomb, M.D.

Page 158	Page 160
<p>1 wrong to say that something is</p> <p>2 consistently shown to be</p> <p>3 associated with something if it's</p> <p>4 not consistently shown.</p> <p>5 And -- and I think for</p> <p>6 statements like that, you can rely</p> <p>7 on what the general population</p> <p>8 would consider consistency, or</p> <p>9 just any reasonable person. So if</p> <p>10 someone says something is a</p> <p>11 hallmark of a disease, and there's</p> <p>12 no good evidence that it is even a</p> <p>13 part of the disease, then, you</p> <p>14 know, that's not a judgment call</p> <p>15 at that point. That's the</p> <p>16 difference between a misstatement</p> <p>17 and a -- it's just a misstatement.</p> <p>18 BY MS. GARBER:</p> <p>19 Q. We will get to the issue of</p> <p>20 consistency, Doctor.</p> <p>21 In addressing -- or in</p> <p>22 assessing -- strike that.</p> <p>23 Do you agree that experts</p> <p>24 can reasonably weigh factors differently?</p>	<p>1 that informs the reader of the</p> <p>2 methodology that you employed to render</p> <p>3 your opinions.</p> <p>4 A. I would have to point to my</p> <p>5 description of the Bradford Hill</p> <p>6 criteria.</p> <p>7 Q. Where does that appear?</p> <p>8 A. I'll find it for you.</p> <p>9 Page 19.</p> <p>10 Q. Doctor, is that a</p> <p>11 methodology section? I asked you</p> <p>12 specifically if you could point me to the</p> <p>13 methodology section.</p> <p>14 A. No. That does -- that is</p> <p>15 not a methodology section.</p> <p>16 Q. And, in fact, you don't have</p> <p>17 a methodology section in your report, do</p> <p>18 you?</p> <p>19 A. I don't have a --</p> <p>20 MS. CURRY: Object to the</p> <p>21 form.</p> <p>22 THE WITNESS: I don't have a</p> <p>23 specific section labeled</p> <p>24 methodology, no.</p>
Page 159	Page 161
<p>1 MS. CURRY: Object to the</p> <p>2 form.</p> <p>3 THE WITNESS: What I was</p> <p>4 trying to get at, and I was hoping</p> <p>5 that we would be able to cover</p> <p>6 this quickly, but probably not.</p> <p>7 That --</p> <p>8 BY MS. GARBER:</p> <p>9 Q. Doctor, just yes or no. And</p> <p>10 you're --</p> <p>11 A. I need -- no --</p> <p>12 Q. -- going to have an</p> <p>13 opportunity for your lawyer to ask you</p> <p>14 questions.</p> <p>15 A. But ma'am, if you ask a</p> <p>16 question --</p> <p>17 MS. GARBER: Object to form.</p> <p>18 BY MS. GARBER:</p> <p>19 Q. I will withdraw the</p> <p>20 question.</p> <p>21 A. Okay.</p> <p>22 Q. Doctor, with regard to</p> <p>23 methodology, will you please point me to</p> <p>24 the methodology section in your report</p>	<p>1 BY MS. GARBER:</p> <p>2 Q. And, in fact, in the four</p> <p>3 corners of your report you do not state</p> <p>4 anywhere the methodology that you</p> <p>5 employed in coming to your opinions. Is</p> <p>6 that also a true statement?</p> <p>7 MS. CURRY: Object to the</p> <p>8 form.</p> <p>9 THE WITNESS: Throughout my</p> <p>10 report, within the four corners</p> <p>11 one could see the methodology I'm</p> <p>12 using. And then I go onto explain</p> <p>13 where I got that methodology with</p> <p>14 Bradford Hill.</p> <p>15 BY MS. GARBER:</p> <p>16 Q. Doctor, you understand the</p> <p>17 methodology is important so that opinions</p> <p>18 can be replicated, right?</p> <p>19 When you're reviewing a</p> <p>20 study, there's a methods section, so that</p> <p>21 the evaluation can be replicated. You</p> <p>22 understand that, right?</p> <p>23 A. Yes.</p> <p>24 MS. CURRY: Object to the</p>

41 (Pages 158 to 161)

Kevin Holcomb, M.D.

Page 162	Page 164
<p>1 form.</p> <p>2 BY MS. GARBER:</p> <p>3 Q. You don't have a methodology</p> <p>4 section in your report where --</p> <p>5 A. I do not.</p> <p>6 Q. Thank you.</p> <p>7 Doctor, if we could move</p> <p>8 onto your statements about plaintiffs'</p> <p>9 criticism of not reviewing the totality</p> <p>10 of the literature.</p> <p>11 I want to ask some questions</p> <p>12 of you.</p> <p>13 You did not review the</p> <p>14 totality of the literature relating to</p> <p>15 biologic plausibility, because you did</p> <p>16 not review the Shukla, Buz'Zard, Saed</p> <p>17 references before rendering your expert</p> <p>18 opinion in the case?</p> <p>19 MS. CURRY: Object to the</p> <p>20 form.</p> <p>21 BY MS. GARBER:</p> <p>22 Q. In -- in this case. Do you</p> <p>23 agree with that?</p> <p>24 MS. CURRY: Object to the</p>	<p>1 the studies that you're referring</p> <p>2 to, I did not specifically mention</p> <p>3 those studies at the time that I</p> <p>4 presented my opinion, because my</p> <p>5 view of the Bradford Hill criteria</p> <p>6 was that there's a reason why the</p> <p>7 first one is strength of</p> <p>8 association and the second is</p> <p>9 consistency. And that I felt that</p> <p>10 my reasoning showing the</p> <p>11 inconsistencies there, that</p> <p>12 it's -- it's an interesting</p> <p>13 question to look at biological</p> <p>14 plausibility and -- and -- but</p> <p>15 when you have such weakness in the</p> <p>16 epidemiologic data, I did not</p> <p>17 spend as much time going through</p> <p>18 the biologic plausibility other</p> <p>19 than to the degree that I did,</p> <p>20 because I think -- and it's full</p> <p>21 of weaknesses there as well.</p> <p>22 But no, my opinion, just</p> <p>23 even based on the epidemiology</p> <p>24 is -- is that there isn't a</p>
Page 163	Page 165
<p>1 form.</p> <p>2 THE WITNESS: I believe that</p> <p>3 even though it's -- I didn't have</p> <p>4 a methodology section, I did</p> <p>5 approach this in a method --</p> <p>6 methodical way --</p> <p>7 BY MS. GARBER:</p> <p>8 Q. Doctor, I didn't ask you</p> <p>9 about your methodology.</p> <p>10 A. If I -- if I can finish my</p> <p>11 answer, please.</p> <p>12 MS. CURRY: Please stop</p> <p>13 cutting him off.</p> <p>14 THE WITNESS: So --</p> <p>15 MS. GARBER: Motion to</p> <p>16 strike.</p> <p>17 BY MS. GARBER:</p> <p>18 Q. My question was about</p> <p>19 Shukla, Buz'Zard and Saez --</p> <p>20 MS. SHARKO: You have to let</p> <p>21 him finish his answer. You are</p> <p>22 not allowed to interrupt. Now be</p> <p>23 polite please.</p> <p>24 THE WITNESS: With regard to</p>	<p>1 consistent finding of an</p> <p>2 association with talc use and</p> <p>3 ovarian cancer.</p> <p>4 BY MS. GARBER:</p> <p>5 Q. Doctor, is it your testimony</p> <p>6 that if you look at the epidemiological</p> <p>7 literature and you find it weak, you</p> <p>8 don't then need to go on and review the</p> <p>9 biologic plausibility to render a</p> <p>10 causation opinion?</p> <p>11 MS. CURRY: Object to the</p> <p>12 form.</p> <p>13 BY MS. GARBER:</p> <p>14 Q. Is that your -- is that your</p> <p>15 opinion?</p> <p>16 A. That is not my opinion.</p> <p>17 Q. Okay.</p> <p>18 A. And that's not what I'm</p> <p>19 saying.</p> <p>20 Q. So -- and, Doctor, you did</p> <p>21 not review studies that looked at the</p> <p>22 biologic plausibility for talc and</p> <p>23 ovarian cancer which included Shukla,</p> <p>24 Buz'Zard, and Saed before signing your</p>

Kevin Holcomb, M.D.

Page 166	Page 168
<p>1 report, correct?</p> <p>2 MS. CURRY: Object to the</p> <p>3 form.</p> <p>4 THE WITNESS: I would argue</p> <p>5 that Buz'Zard is not --</p> <p>6 BY MS. GARBER:</p> <p>7 Q. Doctor, yes or no, did you</p> <p>8 review those or not?</p> <p>9 MS. CURRY: Object to the</p> <p>10 form.</p> <p>11 THE WITNESS: I don't --</p> <p>12 MS. CURRY: Please let him</p> <p>13 finish his response.</p> <p>14 THE WITNESS: You're --</p> <p>15 you're looking for yes or no</p> <p>16 simple answers and you keep --</p> <p>17 BY MS. GARBER:</p> <p>18 Q. I'm not looking for</p> <p>19 paragraphs, Doctor.</p> <p>20 A. -- but -- but you keep</p> <p>21 telling me that you're here to clarify my</p> <p>22 answers. But whenever I get started with</p> <p>23 an answer you cut me off, which makes me</p> <p>24 wonder are you really here to clarify my</p>	<p>1 She's asking him to respond to the</p> <p>2 question.</p> <p>3 And if Dr. Holcomb continues</p> <p>4 not to answer a question, it's an</p> <p>5 appropriate issue to take to</p> <p>6 Judge Pisano and that's what we're</p> <p>7 going to do. So -- so --</p> <p>8 MR. MIZGALA: I want to</p> <p>9 insert here. Because you're</p> <p>10 not -- she's not just asking him</p> <p>11 yes or no about the studies.</p> <p>12 She's characterizing the studies</p> <p>13 in a specific manner and he</p> <p>14 disagrees with that. I think he</p> <p>15 should be able to explain that.</p> <p>16 THE WITNESS: That's exactly</p> <p>17 my feeling about it. It's, the</p> <p>18 question is did I review the</p> <p>19 study --</p> <p>20 BY MS. GARBER:</p> <p>21 Q. Doctor, there's no question</p> <p>22 pending.</p> <p>23 Did you --</p> <p>24 MS. SHARKO: All right. So</p>
Page 167	Page 169
<p>1 answers. Because I can explain to you.</p> <p>2 Buz'Zard --</p> <p>3 Q. I didn't ask you for an</p> <p>4 explanation. I asked you, were they</p> <p>5 listed, yes or no. And your answer was</p> <p>6 no --</p> <p>7 A. Can you go back to your last</p> <p>8 question? Can you go back to the</p> <p>9 question?</p> <p>10 Q. Doctor, you understand I'm</p> <p>11 here to ask questions and you're here to</p> <p>12 answer them.</p> <p>13 A. I'm asking you to repeat</p> <p>14 your question.</p> <p>15 MS. CURRY: Ms. Garber,</p> <p>16 you're not letting him answer the</p> <p>17 question. And please, you can't</p> <p>18 keep talking over each other.</p> <p>19 MS. O'DELL: That's really</p> <p>20 not fair. If she's -- if she's</p> <p>21 asking whether the doctor has</p> <p>22 reviewed a study, that's a yes or</p> <p>23 no question.</p> <p>24 She's not cutting you off.</p>	<p>1 all prior questions are withdrawn.</p> <p>2 MS. GARBER: No --</p> <p>3 MS. SHARKO: She will now</p> <p>4 ask a question and hopefully</p> <p>5 she'll be polite and let you</p> <p>6 answer it. If we have to go to</p> <p>7 the judge about the constant</p> <p>8 interrupting that we've had over</p> <p>9 the last few days, then we will.</p> <p>10 MS. O'DELL: We're here for</p> <p>11 the day. Not for the last few</p> <p>12 days. And the questions aren't</p> <p>13 withdrawn. You're welcome to pose</p> <p>14 a new question.</p> <p>15 And -- and I wanted to say</p> <p>16 for the record the suggestion that</p> <p>17 Ms. Garber is not being polite is</p> <p>18 incorrect, Ms. Sharko.</p> <p>19 MS. SHARKO: I disagree.</p> <p>20 But let's go on.</p> <p>21 There's a lot of silence.</p> <p>22 Are you going to ask a question,</p> <p>23 or are you waiting for the doctor</p> <p>24 to answer the --</p>

43 (Pages 166 to 169)

Kevin Holcomb, M.D.

<p style="text-align: right;">Page 170</p> <p>1 MS. GARBER: I'm going to -- 2 I'm going to ask a question. 3 MS. SHARKO: Great. Thank 4 you. 5 BY MS. GARBER: 6 Q. Doctor, you did not review 7 Dr. Longo's testing of talcum powder 8 products for the presence of asbestos, 9 fibrous talc, heavy metals and the like, 10 correct? 11 A. That's correct. 12 Q. And you did not present or 13 discuss the study design limitations with 14 the cohort studies. Do you agree with 15 that, yes or no? 16 MS. CURRY: Object to the 17 form. 18 THE WITNESS: Please repeat. 19 BY MS. GARBER: 20 Q. Did you -- you did not 21 present and discuss the study design 22 limitations of the cohort studies, yes or 23 no? 24 A. I'd have to read through the</p>	<p style="text-align: right;">Page 172</p> <p>1 MS. CURRY: Object to the 2 form. 3 BY MS. GARBER: 4 Q. Do you mention her 5 reference -- his references with regard 6 to causation? 7 MS. CURRY: Object to the 8 form. 9 THE WITNESS: No. I 10 reference his study, not his 11 discussion section. 12 BY MS. GARBER: 13 Q. Okay. In your critique of 14 plaintiffs' experts' opinions, you do not 15 state the methodology used in coming to 16 those opinions, correct? 17 MS. CURRY: Object to the 18 form. 19 THE WITNESS: I do discuss 20 the methodology that I used. I 21 don't have a methodology section 22 that you discussed. 23 BY MS. GARBER: 24 Q. You don't discuss the</p>
<p style="text-align: right;">Page 171</p> <p>1 report again. I don't remember. 2 Q. You can't answer that 3 question? 4 A. I can't. 5 Q. Okay. Is it true, Doctor 6 that you did not provide a word of 7 analysis in your report regarding the 8 contrary data to your causation opinion 9 specifically with regard to 10 Penninkilampi, Health Canada or the Taher 11 paper? 12 MS. CURRY: Object to the 13 form. 14 BY MS. GARBER: 15 Q. Is that true? 16 A. Please repeat one more time. 17 Q. Your report does not provide 18 a word of analysis regarding the contrary 19 data to your causation opinion, 20 specifically the Penninkilampi, Health 21 Canada or Taher analysis of causation, 22 correct? 23 A. No, I -- I mentioned 24 Penninkilampi.</p>	<p style="text-align: right;">Page 173</p> <p>1 methodology that you employed in 2 rendering critiques of plaintiffs' 3 experts' opinions, correct? 4 MS. CURRY: Object to the 5 form. 6 THE WITNESS: I just discuss 7 and describe my critiques, yes. 8 BY MS. GARBER: 9 Q. Wouldn't you agree, Doctor, 10 that there's medical consensus that the 11 female genital tract is an open system to 12 facilitate the passage of menses and 13 promote retrograde movement of sperm? 14 MS. CURRY: Object to the 15 form. 16 THE WITNESS: Yes. 17 BY MS. GARBER: 18 Q. Let's talk about your 19 opinions and be sure that I understand 20 what they are. 21 These should be yes or no 22 questions, not why. 23 Okay. Is it your opinion 24 that the literature does not provide a</p>

44 (Pages 170 to 173)

Kevin Holcomb, M.D.

<p style="text-align: right;">Page 174</p> <p>1 biologically plausible mechanism whereby 2 talcum powder products can migrate from a 3 woman's genitals to her ovaries? 4 MS. CURRY: Object to the 5 form. 6 THE WITNESS: Is it my 7 opinion that it does not provide? 8 BY MS. GARBER: 9 Q. Correct. 10 A. The answer would be yes. 11 Q. Is it your opinion that the 12 literature does not provide a 13 biologically plausible mechanism whereby 14 talcum powder products can induce chronic 15 inflammation, resulting in ovarian 16 cancer? 17 A. I believe that it proves 18 that it can cause chronic inflammation. 19 I don't believe that it's been proven 20 that that causes ovarian cancer. 21 Q. Is it your opinion that 22 talcum powder products do not increase 23 the risk of developing ovarian cancer? 24 A. Yes.</p>	<p style="text-align: right;">Page 176</p> <p>1 BY MS. GARBER: 2 Q. Is your opinion limited to 3 there's no credible evidence -- 4 MS. CURRY: Object to the 5 form. 6 BY MS. GARBER: 7 Q. -- that talc is associated 8 with ovarian cancer? 9 MS. CURRY: Object to the 10 form. 11 THE WITNESS: This is going 12 to be tough for yes or no. I 13 can't answer that with a yes or 14 no. 15 BY MS. GARBER: 16 Q. Okay. As a gynecologic 17 oncologist, you're a member of the 18 Society For Gynecologic Oncology, right? 19 A. Correct. 20 Q. And you've served as a 21 reviewer for the publications submitted 22 to the Journal of Gynecologic Oncology, 23 right? 24 A. Correct.</p>
<p style="text-align: right;">Page 175</p> <p>1 Q. And if talcum powder 2 products contain asbestos, does that 3 opinion change? 4 A. No. 5 Q. Is it your opinion that 6 talcum powder products do not cause 7 ovarian cancer? 8 A. I don't have an opinion. 9 I'm sorry. Talcum powder is -- did you 10 ask the same question twice? 11 Q. No. One was risk, one was 12 cause. 13 A. Oh. 14 Q. Is it your opinion that 15 talcum powder products do not cause 16 ovarian cancer? 17 A. That's my opinion. 18 Q. Is it your opinion that 19 there is no evidence that talc is 20 associated with ovarian cancer? 21 MS. CURRY: Object to the 22 form. 23 THE WITNESS: No, that's not 24 my opinion.</p>	<p style="text-align: right;">Page 177</p> <p>1 Q. And I assume that you 2 believe the journal -- the journal is a 3 reliable source for study data generally? 4 MS. CURRY: Object to the 5 form. 6 THE WITNESS: What's your 7 definition of reliable? 8 BY MS. GARBER: 9 Q. What do you think it means? 10 A. I don't use that term 11 reliable. So I wouldn't use that term. 12 Q. Do you read the journal? 13 A. Yes, I do. 14 Q. And the data that's 15 contained therein generally, do you deem 16 it reliable for what it provides or do 17 you think it's not credible? 18 MS. CURRY: Object to the 19 form. 20 THE WITNESS: Again, if 21 you're saying I believe it's 22 reliable, do I assume that 23 everybody is honestly reporting 24 what they found, that is a general</p>

45 (Pages 174 to 177)

Kevin Holcomb, M.D.

Page 178	Page 180
<p>1 assumption that we hold in 2 academic medicine. And, yes, I 3 make that assumption for 4 gynecologic oncology. 5 There's no way for a 6 reviewer or someone else to know 7 if someone is giving you false 8 information. We assume it's all 9 valid and that they've not lied 10 about anything. So is that what 11 you mean by reliable? 12 BY MS. GARBER: 13 Q. Have you had an experience 14 as a reviewer for Gynecologic Oncology 15 where authors submitted false data? 16 A. What I'm saying is we don't 17 ask for raw data. I've never -- let me 18 say I. I have never asked a submitting 19 scientist for their raw data so that I 20 could look for irregularities. There is 21 a general understanding that you are 22 trusting the person is giving you their 23 findings, and you're reviewing them with 24 that understanding.</p>	<p>1 Q. Okay. I'm going to show you 2 a paper, Doctor. I don't believe it was 3 cited in your expert report. 4 (Document marked for 5 identification as Exhibit 6 Holcomb-8.) 7 BY MS. GARBER: 8 Q. I'm going to mark as 9 Exhibit 8 -- oh, sorry. 10 Doctor, this is a paper that 11 is published in Gynecologic Oncology 12 titled "Talc and Ovarian Cancer" by 13 Steven Narod, the date of this study is 14 2016. 15 Have you read this paper 16 before? 17 A. I've seen it before, yes. 18 Q. And when did you see it? 19 A. When it came out. 20 Q. Okay. Did you review it as 21 a reviewer for -- 22 A. No. 23 Q. Thank you. Let me -- let me 24 get that clear.</p>
Page 179	Page 181
<p>1 Q. And based on the fact that 2 you're a reviewer for Gynecologic 3 Oncology, do you tend to trust the data 4 presented in that journal? 5 MS. CURRY: Object to the 6 form. 7 THE WITNESS: When you 8 say -- unfortunately, when you say 9 "trust" -- 10 BY MS. GARBER: 11 Q. That was your word, Doctor. 12 A. You may disagree with the 13 findings, but the word -- when I use the 14 word "trust," that's why I keep on coming 15 back to believing that what the person is 16 giving you is valid, this is actually 17 what they did, that they're not 18 falsifying results. To that degree, I 19 trust those results just as much as any 20 other journal. 21 Whether I find the findings 22 of every study valid, no. Just because 23 it's in GYN Oncology does not mean that I 24 take it as a valid study.</p>	<p>1 Did you review this paper 2 prior to its publication attendant to 3 your reviewer role from time to time with 4 Gynecologic Oncology? 5 A. I did not review this paper 6 before publication. 7 Q. Okay. Let's look at some of 8 the statements that are therein. 9 If you look at, Doctor, the 10 bottom of Page 2. The very last sentence 11 at the bottom of Page 2. 12 And, Doctor, it reads: "In 13 any case, given the number of hazard 14 ratios reported in the literature" -- 15 A. I'm -- I'm sorry, I'm 16 looking for you. Bottom of 2. 17 Q. Doctor, you can look up here 18 at the Elmo. 19 A. Yes. 20 Q. And see where I am. I'm at 21 the bottom of 2, Page 2. Left-hand 22 column. 23 A. Okay. Left-hand column. 24 That helps. Okay.</p>

46 (Pages 178 to 181)

Kevin Holcomb, M.D.

Page 182	Page 184
<p>1 Q. And -- and it says, "This 2 article about talc and ovarian cancer 3 indicates in any case given the number of 4 hazard ratios reported in the literature 5 between 1.1 and 1.4 in both case-control 6 and cohort studies, it would be 7 disingenuous to state that there is no 8 evidence that talc is associated with 9 ovarian cancer." 10 Did I read that correctly? 11 A. Yes, you read it correctly. 12 Q. Yes or no, do you agree with 13 that statement? 14 A. It's actually a question you 15 already asked me and I agreed. 16 Q. Let's look at some of the 17 other statements in this paper and see if 18 you agree with them. 19 If you go over to the first 20 page, Doctor, right-hand column. 21 As to the issue of 22 consistency, it indicates, "The 23 case-control studies to date are 24 consistent. Given the small effect size</p>	<p>1 inconsistency. Some are positive and 2 some are negative. 3 So you read it correctly. I 4 think it's a contradictory statement. 5 He's saying they are consistent, and then 6 says some are positive, some are 7 negative. That's not my definition of 8 consistency. 9 Q. Doctor, this study author 10 is -- in a peer-reviewed paper said that 11 the data are consistent. Do you agree 12 with that? 13 A. And then himself says some 14 are positive and some are negative. And 15 I'm asking, my definition of consistency 16 means that they say the same thing. 17 Q. I didn't ask you for what -- 18 why. I said did this study author in a 19 peer-reviewed journal call the data 20 consistent, yes or no? 21 A. Yes. Yes. 22 Q. Thank you. You didn't 23 present that in your expert report that 24 there are peer-reviewed published authors</p>
Page 183	Page 185
<p>1 it is not surprising that some are 2 positive, i.e., show a consistent" -- 3 "show a significant increase in risk and 4 some are negative, i.e., show a 5 nonconsistent increased risk." 6 MS. CURRY: You keep saying 7 consistent, but the word is 8 significant. 9 MS. GARBER: Significant. 10 BY MS. GARBER: 11 Q. Let me start again. 12 "The case-control studies to 13 date are consistent. Given the small 14 effect size it is not surprising that 15 some are positive, i.e., show a 16 significant increased risk and some are 17 negative, i.e., show a nonsignificant 18 increase in risk or no risk difference." 19 Did I read that correctly? 20 A. Yes. 21 Q. Do you disagree with that? 22 A. It's interesting. He says 23 the case-control studies are consistent, 24 and then goes on to describe</p>	<p>1 who say the data are consistent, did you? 2 MS. CURRY: Object to the 3 form. 4 THE WITNESS: I would like 5 to say that this is a -- this -- 6 there's a difference between a 7 paper and a news -- a story in a 8 newspaper that a reporter wrote 9 and an op Ed. 10 This is the medical version 11 of an op Ed. I'm not going to be 12 citing op Eds. I'm going to be 13 citing the literature that's based 14 on. 15 And -- and you find the 16 difficulty with what Dr. Narod is 17 saying here in his own statement. 18 It's contradictory. He could -- 19 it would have made more sense if 20 he said I can explain away the 21 inconsistency. Because the effect 22 size is low you can expect to see 23 inconsistent data. But you can't 24 say it's consistent, some are</p>

47 (Pages 182 to 185)

Kevin Holcomb, M.D.

<p style="text-align: right;">Page 186</p> <p>1 positive, some are negative.</p> <p>2 BY MS. GARBER:</p> <p>3 Q. Doctor, let's -- let's turn</p> <p>4 to Table 1 of your expert report. And</p> <p>5 I'll mark that as Exhibit 9.</p> <p>6 (Document marked for</p> <p>7 identification as Exhibit</p> <p>8 Holcomb-9.)</p> <p>9 BY MS. GARBER:</p> <p>10 Q. And this appears in your</p> <p>11 expert report, correct?</p> <p>12 A. Correct.</p> <p>13 Q. And it is separated by --</p> <p>14 I -- I've produced a color copy, right?</p> <p>15 A. Yes.</p> <p>16 Q. Yeah. And it is -- there</p> <p>17 appears to be shaded studies that appear</p> <p>18 to be in a -- in a blue color; is that</p> <p>19 right?</p> <p>20 A. Correct.</p> <p>21 Q. And then those that are not</p> <p>22 shaded, right?</p> <p>23 A. That's correct.</p> <p>24 Q. And then you have shaded</p>	<p style="text-align: right;">Page 188</p> <p>1 case-control data are unreliable because</p> <p>2 they are inconsistent based on some</p> <p>3 studies lack statistical significance?</p> <p>4 MS. CURRY: Object to the</p> <p>5 form.</p> <p>6 BY MS. GARBER:</p> <p>7 Q. Is that your opinion?</p> <p>8 A. I'm -- no. Please repeat</p> <p>9 that again.</p> <p>10 Q. Sure.</p> <p>11 Is it your opinion that the</p> <p>12 case-control data are unreliable because</p> <p>13 they are inconsistent based on some</p> <p>14 studies lack statistical significance?</p> <p>15 A. No. It's my opinion that</p> <p>16 it's not reliable because those studies</p> <p>17 that lack statistical significance are</p> <p>18 actually showing no increased risk, no --</p> <p>19 no -- we -- we use statistical</p> <p>20 significance to say that that increased</p> <p>21 risk was more than just by chance. So</p> <p>22 the lack of statistical significance is</p> <p>23 what leads to the inconsistency.</p> <p>24 Q. Okay. So you believe that</p>
<p style="text-align: right;">Page 187</p> <p>1 the -- some of the studies in blue and</p> <p>2 why are those studies shaded in blue?</p> <p>3 A. They are shaded in blue,</p> <p>4 because they have 95 -- 95 percent</p> <p>5 confidence intervals that cross one. And</p> <p>6 that is not a statistically significant</p> <p>7 finding whether it's showing an increase</p> <p>8 or a decrease.</p> <p>9 Q. Did you create this table?</p> <p>10 A. Yes, I did.</p> <p>11 Q. On your computer?</p> <p>12 A. Yes.</p> <p>13 Q. And you put all the data</p> <p>14 into this table and -- and color-coded</p> <p>15 it?</p> <p>16 A. Yes.</p> <p>17 Q. In your expert report at</p> <p>18 Page 10, you indicate that the -- with</p> <p>19 regard to the case-control studies, the</p> <p>20 risk estimates range between 1.2 and 1.6,</p> <p>21 suggesting a 20 to 60 percent increased</p> <p>22 risk; is that right?</p> <p>23 A. Yes.</p> <p>24 Q. And so, you believe that the</p>	<p style="text-align: right;">Page 189</p> <p>1 the case-control studies are inconsistent</p> <p>2 because some of the studies don't show</p> <p>3 statistical significance because the</p> <p>4 confidence interval crosses one; is that</p> <p>5 fair?</p> <p>6 A. In the materials and</p> <p>7 methods, like you asked me to have a</p> <p>8 methods section, they will say before</p> <p>9 they look at the data, and this is what</p> <p>10 you do, so you're not biased, you say</p> <p>11 we're going to consider this significant</p> <p>12 at this level. We're going to consider</p> <p>13 this a positive study at this level, and</p> <p>14 then you go and you do your analysis.</p> <p>15 And when it doesn't reach that level,</p> <p>16 whether it's above or below, you don't</p> <p>17 come out of that study saying there's</p> <p>18 a -- there's a significant risk of</p> <p>19 ovarian cancer associated with talc.</p> <p>20 So everything that's shaded</p> <p>21 in blue, those things are negative</p> <p>22 studies.</p> <p>23 Q. Doctor, do you remember my</p> <p>24 question?</p>

Kevin Holcomb, M.D.

<p style="text-align: right;">Page 190</p> <p>1 A. I felt the need to clarify 2 why I think this is inconsistent. It's 3 not just -- it's because yes, they 4 don't -- they -- they -- 5 Q. Doctor, excuse me. 6 A. Yes. 7 Q. I'm going to interrupt you 8 there, because -- 9 MS. SHARKO: You can't do 10 that. 11 BY MS. GARBER: 12 Q. I -- you -- you understood 13 my question, yet you felt the need to 14 clarify. 15 That isn't what I've asked 16 you to do. I've asked you a very simple 17 question: What's the nature of this 18 Table 1, and then you launched into what 19 the study authors do. 20 A. I -- I think I might be 21 mistaken about the purpose of this -- 22 MS. CURRY: Ms. Garber -- 23 hold on. Can I just state an 24 objection on the record, please?</p>	<p style="text-align: right;">Page 192</p> <p>1 because they're inconsistent with those 2 that do show statistical significance? 3 MS. CURRY: Object to the 4 form. 5 THE WITNESS: Because they 6 are inconsistent with -- no. 7 BY MS. GARBER: 8 Q. Okay. Doctor, if we look at 9 Table 1, with the exception of, I think, 10 two studies, every one of those relative 11 risks are all to the right of one, are 12 they not? 13 A. Yes. 14 Q. And you have odds ratio, 15 relative risk. Which is it for the 16 case-control studies? 17 MS. CURRY: Object to the 18 form. 19 BY MS. GARBER: 20 Q. Which would be proper? 21 A. An odds ratio. 22 Q. Okay. And so -- 23 A. I'm sorry. Hold on. I'm 24 sorry. One second. I'm sorry. It's the</p>
<p style="text-align: right;">Page 191</p> <p>1 THE WITNESS: Okay. 2 MS. SHARKO: The question, 3 if he can't answer it without 4 clarifying, then he's entitled to 5 clarify the question. 6 And the question was broader 7 than what you just stated. It 8 was, because it asked specifically 9 whether or not the case-control 10 studies are inconsistent because 11 it doesn't show statistical 12 significance. 13 BY MS. GARBER: 14 Q. Doctor, is it your opinion 15 that the studies that do not show 16 statistical significance are unreliable 17 and attributable to chance? 18 A. Yes. 19 Q. And is it your opinion that 20 the case-control studies that do not 21 show -- strike that. 22 Is it your opinion that the 23 studies do not -- that do not show 24 statistical significance are unreliable</p>	<p style="text-align: right;">Page 193</p> <p>1 other way around. Case-control would be 2 relative risk. 3 Q. Are you sure? 4 A. Yeah. 5 Q. And all of those studies are 6 to the right of one except two, right? 7 A. Right. 8 Q. And so all of those are 9 positive because they're to the right of 10 one, correct? 11 A. No, that's -- 12 MS. CURRY: Object to the 13 form. 14 THE WITNESS: That's a 15 misunderstanding of statistics. 16 They are not positive because 17 they're to the right of one. It's 18 defined in the study what they 19 were going to consider a positive 20 study. It had to be above one and 21 have a 95 percent chance that the 22 true risk estimate was within the 23 range of the 95 percent confidence 24 interval. So once it drops below</p>

Kevin Holcomb, M.D.

<p style="text-align: right;">Page 194</p> <p>1 one, you're saying the author 2 themselves, by doing the 3 statistics, by putting that in the 4 materials and methods, they're 5 saying I don't consider this a 6 positive study unless I achieve a 7 positive direction above one and 8 the 95 percent confidence interval 9 does not cross one, otherwise why 10 bother doing that? 11 BY MS. GARBER: 12 Q. Can you give me any article, 13 treatise, authority, that supports that 14 claim that for a study to be positive, it 15 needs to be greater than one and reach 16 statistical significance? 17 A. Any treatise? 18 Q. Any -- any authority to 19 support that claim? 20 A. Again, I think for each 21 individual paper, I could go through the 22 materials and methods, and the author who 23 wrote that paper will describe, before 24 they started collecting data, their</p>	<p style="text-align: right;">Page 196</p> <p>1 off the top of your head? 2 A. No. It's such -- you're 3 asking something that is so widely 4 accepted, that it would be like finding 5 an authority that says water is H2O. I 6 mean, it's -- I could find a nice review 7 article that explains, and this all comes 8 down to the quality of the study, and in 9 the study design how much risk is there 10 for a spurious value, for a confounder or 11 for a recall bias to play a role. 12 And that's why you have -- I 13 think of 95 confidence intervals as your 14 bumpers, your safety bumpers that keep 15 you from making a mistake. 16 Q. Is the point estimate the 17 best estimate of risk? 18 MS. CURRY: Object to the 19 form. 20 THE WITNESS: The point 21 estimate has to be taken into 22 account with the 95 percent 23 confidence intervals. 24 BY MS. GARBER:</p>
<p style="text-align: right;">Page 195</p> <p>1 methodology. And what they were going to 2 consider significant. 3 Q. Do you understand that to be 4 authority? 5 MS. CURRY: Object to the 6 form. 7 THE WITNESS: I'm saying for 8 each individual person that's 9 doing the study, that is their 10 definition of what they considered 11 a positive study. 12 BY MS. GARBER: 13 Q. I understand that. I'm 14 asking you for an authoritative paper 15 that indicates your definition of a 16 positive study meaning greater than one 17 that reached statistical significance 18 constitutes a positive study. Can you 19 please give me an authority for that 20 statement? 21 A. I'm sure if you gave me the 22 time I could find it. But I don't have 23 one that I can quote you now. 24 Q. You can't come up with one</p>	<p style="text-align: right;">Page 197</p> <p>1 Q. That wasn't my question. Is 2 the point estimate the best estimate of 3 risk? 4 MS. CURRY: Object to the 5 form. 6 THE WITNESS: I don't 7 understand your question. As 8 opposed to what? 9 BY MS. GARBER: 10 Q. In looking at the data, in 11 looking -- 12 A. As opposed to what though? 13 All you get is the point estimate and the 14 95 percent confidence interval. So 15 you're saying it's better than what? 16 Q. You've never seen that 17 statement that the point estimate is the 18 best estimate of risk? 19 A. Have you heard the term 20 "compared to what"? 21 Q. Okay. Doctor, what is your 22 definition of a negative study? 23 A. A negative study is a study 24 that doesn't reach your predefined</p>

50 (Pages 194 to 197)

Kevin Holcomb, M.D.

Page 198	Page 200
<p>1 definition of a positive study. Anything 2 that doesn't reach your definition of a 3 positive study -- there's no in between. 4 It's either positive or negative. 5 Q. So your definition of 6 negative is a study which can be to the 7 right of one or greater than one, but 8 doesn't reach statistical significance? 9 That's how -- 10 A. Say this once again. 11 Q. That's how you define a 12 negative study? 13 MS. CURRY: Object to the 14 form. 15 THE WITNESS: I do. And the 16 reason being is because when you 17 think about the problems with 18 case-control studies, and it's 19 every -- all the experts on both 20 sides talk about this risk of 21 recall bias. Recall bias never 22 sends your numbers below zero. 23 BY MS. GARBER: 24 Q. Doctor, did I ask you about</p>	<p>1 Holcomb-10.) 2 BY MS. GARBER: 3 Q. I'm going to mark as 4 Exhibit 10 a paper that was just 5 published. Doctor, in just looking at 6 this paper -- this paper was just 7 published on March 21st, here at the 8 bottom. March 21, 2019, in Nature. 9 Do you -- do you know that 10 journal? 11 A. Yes. 12 Q. And what's your opinion of 13 that journal? 14 A. Nature? 15 Q. Mm-hmm. 16 A. It's a highly respected 17 journal. 18 Q. Thank you. 19 And do you see that the 20 title of this article is "Retire 21 Statistical Significance"? 22 A. Yes. And this is a comment 23 in the highly respected journal. Again, 24 this is an op Ed piece, not -- this is</p>
Page 199	Page 201
<p>1 recall bias? 2 A. And I'm explaining why I 3 have this opinion. 4 Q. I didn't ask you why you 5 have your opinion. 6 A. Then I'll withdraw my 7 statement. 8 Q. Your lawyer will be able to 9 ask you questions. Thank you, Doctor. 10 Doctor, have you cited any 11 authority to support your claims that 12 studies that don't show statistical 13 significance are attributable to chance 14 and bias? 15 A. No. That's not -- that's 16 not my claim, first of all. 17 Q. Okay. Doctor, do you know 18 who Sander Greenland is? 19 A. No. 20 Q. Do you know who Kenneth 21 Rothman is? 22 A. No. 23 (Document marked for 24 identification as Exhibit</p>	<p>1 not a study. 2 Q. Doctor, do you see who the 3 study authors are? 4 A. Yes. 5 Q. And do you see that Sander 6 Greenland is one of the study authors? 7 A. Yes. 8 Q. And do you see that it goes 9 on to say, "And more than 800 signatories 10 call for an end to the hyped claim and 11 dismissal of possibly crucial effects." 12 Do you see that? That's 13 the -- 14 A. Yes, I do see that. 15 Q. All right. And let's look 16 at this paper, if we could, together. 17 It begins by stating, "When 18 was the last time you heard a seminar 19 speaker claim that there was no 20 difference between two groups because the 21 difference was statistically 22 nonsignificant?" 23 Did I read that correctly? 24 A. You read that correctly.</p>

51 (Pages 198 to 201)

Kevin Holcomb, M.D.

<p style="text-align: right;">Page 202</p> <p>1 Q. So this is a paper, just</p> <p>2 from the introduction at least, looking</p> <p>3 like it's going to talk about statistical</p> <p>4 versus non-statistical data using the</p> <p>5 95 percent confidence interval, right?</p> <p>6 A. Right.</p> <p>7 MS. CURRY: Object to the</p> <p>8 form.</p> <p>9 BY MS. GARBER:</p> <p>10 Q. Is that fair?</p> <p>11 And then if you go to the</p> <p>12 section which indicates the pervasive</p> <p>13 problem. It says, "Let's be clear about</p> <p>14 what must stop. We should never conclude</p> <p>15 that there is no difference or no</p> <p>16 association just because a P-value is</p> <p>17 larger than a threshold such as 2</p> <p>18 point" -- "such as 0.05."</p> <p>19 And then we turn to the next</p> <p>20 page, "or equivocally because a</p> <p>21 confidence interval includes zero."</p> <p>22 MS. CURRY: Take the time to</p> <p>23 look it through.</p> <p>24 BY MS. GARBER:</p>	<p style="text-align: right;">Page 204</p> <p>1 It is equally absurd to claim that these</p> <p>2 results were in contrast with earlier</p> <p>3 results showing an identical observed</p> <p>4 result, yet these common practices show</p> <p>5 how reliance on thresholds of statistical</p> <p>6 significance can" -- "can mislead us (See</p> <p>7 'Beware false conclusions')."</p> <p>8 Did I read that correctly?</p> <p>9 A. You did.</p> <p>10 Q. And -- and that's, in fact,</p> <p>11 what you've done in Table 1, haven't you?</p> <p>12 MS. CURRY: Object to the</p> <p>13 form.</p> <p>14 BY MS. GARBER:</p> <p>15 Q. You've tried to separate</p> <p>16 them by statistically significant and</p> <p>17 nonstatistically significant, correct?</p> <p>18 A. As -- as much -- I did</p> <p>19 divide them by significance and</p> <p>20 nonsignificance.</p> <p>21 Based on these doctors --</p> <p>22 I'm not familiar with them. But they are</p> <p>23 clearly worried about missing significant</p> <p>24 effects that are small, and I'm not</p>
<p style="text-align: right;">Page 203</p> <p>1 Q. "Neither should we include</p> <p>2 that two studies conflict because one has</p> <p>3 a statistically significant result and</p> <p>4 the other did not. These errors waste</p> <p>5 research efforts and misinform policy</p> <p>6 decisions."</p> <p>7 Did I read that correctly,</p> <p>8 Doctor?</p> <p>9 A. Yes, you read that</p> <p>10 correctly.</p> <p>11 Q. That's the opinion of these</p> <p>12 authors and 800 signatories, correct?</p> <p>13 MS. CURRY: Object to the</p> <p>14 form.</p> <p>15 THE WITNESS: I haven't read</p> <p>16 the full paper, but that's what</p> <p>17 the title says, yes.</p> <p>18 BY MS. GARBER:</p> <p>19 Q. All right. Let's go on to</p> <p>20 read further down where it indicates, "It</p> <p>21 is ludicrous to conclude that the</p> <p>22 statistically nonsignificant results</p> <p>23 showed no association when the interval</p> <p>24 estimate included serious risk increases.</p>	<p style="text-align: right;">Page 205</p> <p>1 saying I'm not interested in small effect</p> <p>2 sizes. But I'm saying that because of</p> <p>3 the risk of -- of confounders and other</p> <p>4 biases, that you need to find -- if</p> <p>5 you're going to have a small effect size,</p> <p>6 you're going to need to find consistency</p> <p>7 along -- the -- the onus is going to be</p> <p>8 even stronger to prove that you're not</p> <p>9 making a spurious conclusion. Because I</p> <p>10 would imagine, being Nature contributors,</p> <p>11 these are likely basic science</p> <p>12 researchers. And I can show you example</p> <p>13 after example in clinical medicine where</p> <p>14 nonsignificant findings led to wrong</p> <p>15 results. Whether -- and I give some</p> <p>16 examples in my report with, you know,</p> <p>17 what causes cervix cancer, the effect of</p> <p>18 estrogen replacement therapy. These</p> <p>19 things that we did not use the safety</p> <p>20 bumpers of 95 percent confidence</p> <p>21 intervals. It just -- it doesn't mean</p> <p>22 that the studies should stop. It just</p> <p>23 means -- and that you have a definitive</p> <p>24 answer. It means that that should raise</p>

Kevin Holcomb, M.D.

Page 206	Page 208
<p>1 questions for you and that should make 2 you think that there may be something 3 else going on. 4 MS. GARBER: Objection. 5 Motion to strike as nonresponsive. 6 BY MS. GARBER: 7 Q. Doctor, what we're talking 8 about here is ovarian cancer, correct? 9 A. Correct. 10 Q. We're talking about a risk 11 of a deadly disease, correct? 12 A. I treat ovarian cancer, 13 ma'am. We don't have to go through the 14 fact it's deadly. 15 Q. Right. And -- and so here 16 there is a body of literature over 17 40 years that's looked at the topic, 18 right? 19 A. Right. 20 Q. And that body of literature 21 has consistent odds ratios throughout 22 case-control, cohort and -- and 23 meta-analyses? 24 A. Cohort, no --</p>	<p>1 that he is a plaintiffs' expert 2 here? I'm just curious. 3 MS. GARBER: Let's -- let's 4 go on. 5 BY MS. GARBER: 6 Q. Doctor -- 7 MS. O'DELL: Susan, that's 8 totally inappropriate. Stop 9 coaching the witness. 10 MS. SHARKO: I'm not. I'm 11 not coaching him. I'm asking you. 12 MS. O'DELL: He's not my 13 expert. I don't know what you're 14 talking about. 15 MS. SHARKO: You identified 16 him as an plaintiffs' expert. 17 MS. O'DELL: I did not. 18 MS. SHARKO: Yeah, you did. 19 Look at your disclosures. 20 All right. We'll send -- 21 we'll send you a letter on this, 22 because I'm concerned about that. 23 MS. GARBER: So I -- I would 24 just like to say I would</p>
Page 207	Page 209
<p>1 MS. CURRY: Object to the 2 form. 3 THE WITNESS: I disagree 4 with that. 5 BY MS. GARBER: 6 Q. You do? 7 A. Yeah. 8 Q. Okay. The cohort studies 9 are showing, aside from the Gonzalez 10 study, they are all showing numbers that 11 are to the right of one, aren't they? 12 MS. CURRY: Object to the 13 form. 14 BY MS. GARBER: 15 Q. For every use? 16 A. For example, Gates is 1.06. 17 Q. Mm-hmm. That's to the right 18 of one, isn't it? 19 A. Yes, ma'am. Just right to 20 the right of one. 21 Q. Okay. Let's -- let's carry 22 on with this paper. 23 MS. SHARKO: Why doesn't -- 24 why doesn't Dr. Greenland disclose</p>	<p>1 appreciate it, Ms. Sharko, if you 2 could stop coaching. I understand 3 your need to, you know, speak up, 4 but Ms. Curry is completely 5 capable of defending the doctor. 6 And your coaching only frustrates 7 the process. 8 And -- and I will go to the 9 Court if we need to, because it's 10 not fair. And you know it. 11 MS. SHARKO: Right. There's 12 no coaching. I asked you -- 13 MS. GARBER: There is 14 coaching, Ms. Sharko. You -- you 15 have just coached him about 16 Dr. Greenland, so -- 17 MS. SHARKO: You are 18 interrupting me. You are 19 interrupting me. 20 MS. GARBER: Because, you 21 know what, we're on the record. 22 So we'll have this topic off the 23 record later if we like. 24 MS. SHARKO: Are you going</p>

53 (Pages 206 to 209)

Kevin Holcomb, M.D.

Page 210	Page 212
<p>1 to interrupt me off the record?</p> <p>2 There's no question pending.</p> <p>3 It's a question for the plaintiffs</p> <p>4 and we'll pursue it. We'll pursue</p> <p>5 it off the record.</p> <p>6 BY MS. GARBER:</p> <p>7 Q. Doctor, could you look at</p> <p>8 the bottom of this document. And it</p> <p>9 indicates: "Beware of false conclusions.</p> <p>10 Studies currently dubbed statistically</p> <p>11 significant and statistically</p> <p>12 nonsignificant need not be contradictory,</p> <p>13 and as such, designations might cause</p> <p>14 genuine effects to be dismissed."</p> <p>15 Do you see that?</p> <p>16 A. Yes.</p> <p>17 Q. The study authors are very</p> <p>18 concerned about risk of disease being</p> <p>19 dismissed because a body of literature</p> <p>20 shows statistical significance and</p> <p>21 another one showing near statistical</p> <p>22 significance, but experts like you,</p> <p>23 dismissing that risk, they are concerned</p> <p>24 about that, aren't they?</p>	<p>1 A. So I'm here to give you my</p> <p>2 opinions --</p> <p>3 Q. I don't --</p> <p>4 A. -- but you're not -- you're</p> <p>5 not really interested in my opinions --</p> <p>6 Q. What I --</p> <p>7 A. -- because every time I try</p> <p>8 to offer it to you, you cut me off and</p> <p>9 you want me to tell you, are you reading</p> <p>10 his opinions correctly.</p> <p>11 Q. No, Doctor, I'm asking for</p> <p>12 yours.</p> <p>13 A. I believe you can read it.</p> <p>14 Q. Do you agree with that?</p> <p>15 That was my question. Do you agree with</p> <p>16 these study authors?</p> <p>17 A. Can you repeat the</p> <p>18 statement?</p> <p>19 Q. Okay. Do you agree with</p> <p>20 these -- strike that.</p> <p>21 These study authors are</p> <p>22 concerned about dismissing genuine</p> <p>23 effects.</p> <p>24 A. Do I agree that they're</p>
Page 211	Page 213
<p>1 A. Because I'm -- I'm</p> <p>2 concerned --</p> <p>3 MR. MIZGALA: Object to the</p> <p>4 form.</p> <p>5 MS. CURRY: Object to the</p> <p>6 form.</p> <p>7 THE WITNESS: What I'm</p> <p>8 concerned about is if you have a</p> <p>9 group of studies that are all the</p> <p>10 same design that are subject --</p> <p>11 BY MS. GARBER:</p> <p>12 Q. Doctor, I didn't ask you</p> <p>13 that. I asked you yes or no, is that the</p> <p>14 author's conclusions in your opinion?</p> <p>15 MR. MIZGALA: Object to the</p> <p>16 form.</p> <p>17 THE WITNESS: The author is</p> <p>18 not here speaking in front of the</p> <p>19 camera. I'm here because you</p> <p>20 asked me my opinions. And if you</p> <p>21 want me to just read their</p> <p>22 opinions, you don't need me here.</p> <p>23 BY MS. GARBER:</p> <p>24 Q. I don't want that. I --</p>	<p>1 concerned?</p> <p>2 Q. Yes.</p> <p>3 MR. MIZGALA: Object to the</p> <p>4 form.</p> <p>5 MS. CURRY: Object to the</p> <p>6 form.</p> <p>7 THE WITNESS: They're</p> <p>8 obviously concerned. They wrote</p> <p>9 the paper.</p> <p>10 BY MS. GARBER:</p> <p>11 Q. Okay. That was my first</p> <p>12 question --</p> <p>13 A. Right.</p> <p>14 Q. -- you didn't answer. Now</p> <p>15 my second question is --</p> <p>16 MS. SHARKO: Objection.</p> <p>17 MS. GARBER: Strike my</p> <p>18 second question. Let's move on.</p> <p>19 MS. SHARKO: Thank you.</p> <p>20 MS. GARBER: You know what?</p> <p>21 I just -- I don't think I've ever</p> <p>22 had another lawyer treat me as</p> <p>23 disrespectfully as you,</p> <p>24 Ms. Sharko. I just can't believe</p>

Kevin Holcomb, M.D.

Page 214	Page 216
<p>1 it. Okay.</p> <p>2 MS. SHARKO: I have great</p> <p>3 respect for you, Ms. Garber. It's</p> <p>4 not my intention to make you feel</p> <p>5 disrespected.</p> <p>6 MS. GARBER: When you laugh</p> <p>7 and you make snide comments, it's</p> <p>8 hard to see that you have great</p> <p>9 respect for me.</p> <p>10 MS. SHARKO: I haven't</p> <p>11 laughed or made snide comments,</p> <p>12 but let's move on.</p> <p>13 BY MS. GARBER:</p> <p>14 Q. Okay. If we move on to the</p> <p>15 middle of the column. The authors say,</p> <p>16 "We agree on the call for the entire</p> <p>17 concept of statistical significance to be</p> <p>18 abandoned. We are far from alone." And</p> <p>19 it goes onto describe, 250 people signed</p> <p>20 on in the first 24 hours and another 800</p> <p>21 experts.</p> <p>22 Do you see that?</p> <p>23 A. Yes.</p> <p>24 Q. And so it's not just these</p>	<p>1 A. I do.</p> <p>2 Q. And you're drawing</p> <p>3 categorical differences in the data</p> <p>4 between statistically significant and</p> <p>5 non-statistically significant, correct?</p> <p>6 MS. CURRY: Object to the</p> <p>7 form.</p> <p>8 THE WITNESS: Will I be able</p> <p>9 to explain for my reasons doing</p> <p>10 so? Or are just going to see if I</p> <p>11 agree with everything that they</p> <p>12 say?</p> <p>13 BY MS. GARBER:</p> <p>14 Q. You know what? Your lawyer</p> <p>15 can ask you questions --</p> <p>16 A. Okay.</p> <p>17 Q. -- that you want asked of</p> <p>18 you --</p> <p>19 A. Okay.</p> <p>20 Q. -- Doctor. But this is my</p> <p>21 opportunity to ask you questions that I</p> <p>22 want to ask you.</p> <p>23 A. Sure.</p> <p>24 Q. And finally, turning over to</p>
Page 215	Page 217
<p>1 study authors. It's -- it's other</p> <p>2 experts in the field, right?</p> <p>3 MS. CURRY: Object to the</p> <p>4 form.</p> <p>5 BY MS. GARBER:</p> <p>6 Q. Do you understand that from</p> <p>7 reading this or do you need to read the</p> <p>8 whole paper?</p> <p>9 MS. CURRY: Object to the</p> <p>10 form.</p> <p>11 THE WITNESS: I agree that</p> <p>12 you read the segment correctly.</p> <p>13 BY MS. GARBER:</p> <p>14 Q. Okay. And then, Doctor,</p> <p>15 finally, under -- at the right-hand side</p> <p>16 under the heading "Quit Categorizing,"</p> <p>17 the authors write, "The trouble is human</p> <p>18 and cognitive more than statistical.</p> <p>19 Bucketing results into statistical</p> <p>20 significance and statistical</p> <p>21 non-significance makes people think that</p> <p>22 the items assigned in the way" -- "in</p> <p>23 that way are categorically different."</p> <p>24 Do you see that?</p>	<p>1 the next page. The -- under the heading</p> <p>2 of "Wrong Interpretations," it reads, "An</p> <p>3 analysis of 791 articles across five</p> <p>4 journals found that around half</p> <p>5 mistakenly assume non-significance means</p> <p>6 no effect."</p> <p>7 Did I read that correctly?</p> <p>8 A. Yes.</p> <p>9 Q. And so, finally, turning</p> <p>10 over to page -- to the right-hand column,</p> <p>11 the authors conclude, "But eradicating</p> <p>12 categorization will help to halt</p> <p>13 overconfident claims, unwarranted</p> <p>14 declarations of no difference, and absurd</p> <p>15 statements about replication failure when</p> <p>16 the results from the original and</p> <p>17 replication studies are highly</p> <p>18 compatible.</p> <p>19 "The misuse of statistical</p> <p>20 significance has done much harm to the</p> <p>21 science community and those who rely on</p> <p>22 scientific evidence. P-values, intervals</p> <p>23 and other statistical measures all have</p> <p>24 their place, but it's time for</p>

55 (Pages 214 to 217)

Kevin Holcomb, M.D.

<p style="text-align: right;">Page 218</p> <p>1 statistical significance to go." 2 And I assume that you 3 disagree with these 800-some authors? 4 MS. CURRY: Object to the 5 form. 6 THE WITNESS: If you say 7 P-value has its place, what is its 8 place if not to determine 9 significance? That's all a 10 P-values is. So I would want to 11 know from the authors, if P-values 12 have their place and it's not in 13 determining significance, what 14 exactly is the place for a 15 P-value? It's only used for one 16 thing, determining significance. 17 BY MS. GARBER: 18 Q. What was my question, 19 Doctor? 20 A. I'm sorry. 21 Q. What was my question? 22 A. I don't remember. 23 Q. Okay. My question was, I 24 assume you disagree with those authors;</p>	<p style="text-align: right;">Page 220</p> <p>1 sorry. They want to get rid of 2 statistical significance altogether. 3 Q. You read Health Canada? 4 A. Yes. 5 Q. Let's look at what Health 6 Canada said about the consistency of the 7 study data. Okay? 8 A. Are you going to provide 9 something? 10 Q. I'm going to mark the Health 11 Canada draft screening assessment dated 12 December 2010 as Exhibit 11. 13 A. Thank you. 14 (Document marked for 15 identification as Exhibit 16 Holcomb-11.) 17 BY MS. GARBER: 18 Q. There, Doctor, the study 19 authors indicated that, "The 20 meta-analyses of the available human 21 studies in the peer-reviewed literature 22 indicate a consistent and statistically 23 significant positive association between 24 perineal exposure to talc and ovarian</p>
<p style="text-align: right;">Page 219</p> <p>1 is that correct? 2 A. Yes. 3 Q. So in accord with the study 4 authors of the paper we just reviewed, 5 the case-control data as presented in 6 your Table 1 should not be deemed 7 different or inconsistent based on the 8 confidence interval under the authority 9 of the paper we just reviewed, correct? 10 MS. CURRY: Object to the 11 form. 12 THE WITNESS: Under my 13 authority, I would say they should 14 be considered different. 15 BY MS. GARBER: 16 Q. Under the authority of the 17 paper that we just reviewed -- 18 A. Oh, these doctors want to 19 get rid of statistics altogether. So we 20 wouldn't even -- yeah, they would say 21 don't bother doing them. 22 Q. Where do you see that these 23 doctors want to get rid of statistics? 24 A. Statistical significance,</p>	<p style="text-align: right;">Page 221</p> <p>1 cancer." 2 Do you agree with that, that 3 that's what the meta-analyses show? 4 A. Yes. 5 Q. You disagree? 6 MS. CURRY: Object to the 7 form. 8 BY MS. GARBER: 9 Q. You think -- 10 A. No. They're talking about 11 the meta-analyses? 12 Q. Yes. Do you agree with 13 that? 14 A. I believe they take a bunch 15 of studies, put them together. Yes, 16 that's true. 17 Q. So you believe that they are 18 consistent? 19 A. The meta-analyses? 20 Q. Yes. 21 MS. CURRY: Object to the 22 form. 23 THE WITNESS: The 24 meta-analyses -- if -- if I -- I</p>

56 (Pages 218 to 221)

Kevin Holcomb, M.D.

Page 222	Page 224
<p>1 want to make sure it's okay for me</p> <p>2 to expound on this.</p> <p>3 The meta-analyses combine</p> <p>4 both case-control and cohort</p> <p>5 studies and come to the conclusion</p> <p>6 that the case-control studies that</p> <p>7 they are including, find a</p> <p>8 difference, and usually typically</p> <p>9 described as moderate -- a -- a</p> <p>10 weak difference. And cohort</p> <p>11 studies which show no difference.</p> <p>12 And they combine them together.</p> <p>13 The few that have kept them</p> <p>14 separate and look separately have</p> <p>15 shown no difference in the cohort</p> <p>16 studies they've put together and a</p> <p>17 difference in the case-control</p> <p>18 studies.</p> <p>19 BY MS. GARBER:</p> <p>20 Q. Doctor, the authors here in</p> <p>21 the Health Canada have concluded that the</p> <p>22 meta-analyses are consistent. Do you</p> <p>23 agree with that?</p> <p>24 A. Yes. That's what they are</p>	<p>1 just get into this. I'm half into</p> <p>2 it.</p> <p>3 I'll mark the Taher 2018</p> <p>4 meta-analyses as Exhibit 12.</p> <p>5 (Document marked for</p> <p>6 identification as Exhibit</p> <p>7 Holcomb-12.)</p> <p>8 BY MS. GARBER:</p> <p>9 Q. And turning -- as to the</p> <p>10 topic of consistency, turning over to</p> <p>11 Page 49, under the conclusion, it</p> <p>12 reads --</p> <p>13 A. Page 49, I'm sorry.</p> <p>14 Q. -- "Consistent with previous</p> <p>15 evaluations, the IARC in 2010 and</p> <p>16 subsequent evaluations by individual</p> <p>17 investigators, the present comprehensive</p> <p>18 evaluation of all currently available</p> <p>19 relevant data indicates that perineal</p> <p>20 exposure to talcum powder is a possible</p> <p>21 cause of ovarian cancer in humans."</p> <p>22 First, did I read that</p> <p>23 correctly?</p> <p>24 A. You did read it correctly.</p>
Page 223	Page 225
<p>1 concluding.</p> <p>2 Q. Do you agree with the study</p> <p>3 authors?</p> <p>4 MS. CURRY: Object to the</p> <p>5 form.</p> <p>6 THE WITNESS: Again --</p> <p>7 BY MS. GARBER:</p> <p>8 Q. Do you think they're -- do</p> <p>9 you think they are consistent or</p> <p>10 inconsistent?</p> <p>11 A. No. Meta-analyses are</p> <p>12 consistent.</p> <p>13 Q. Thank you.</p> <p>14 You reviewed the Taher</p> <p>15 paper?</p> <p>16 A. The what?</p> <p>17 Q. The Taher, T-A-H-E-R.</p> <p>18 A. Taher --</p> <p>19 Q. Yes.</p> <p>20 A. -- yes. Mm-hmm.</p> <p>21 MS. CURRY: Ms. Garber,</p> <p>22 whenever it's appropriate to take</p> <p>23 a lunch break?</p> <p>24 MS. GARBER: Okay. Let me</p>	<p>1 Q. And this indicates that the</p> <p>2 data are consistent --</p> <p>3 MS. CURRY: Object to the</p> <p>4 form.</p> <p>5 BY MS. GARBER:</p> <p>6 Q. -- correct?</p> <p>7 A. It's consistent with IARC,</p> <p>8 yes.</p> <p>9 Q. Does it limit it to IARC,</p> <p>10 that statement?</p> <p>11 A. IARC is basically using the</p> <p>12 subsequent evaluations and so consistency</p> <p>13 would not be surprising when you're</p> <p>14 rechurning the same data over and over.</p> <p>15 So when you say that the --</p> <p>16 the individual investigators are</p> <p>17 consistent with IARC, but IARC uses</p> <p>18 individual investigators. When you have</p> <p>19 individual investigator's data then put</p> <p>20 together into a pooled analysis, you</p> <p>21 would expect consistency. When you --</p> <p>22 when you do meta-analysis that then take</p> <p>23 those same individual studies and put all</p> <p>24 the patients together, you would expect</p>

57 (Pages 222 to 225)

Kevin Holcomb, M.D.

Page 226	Page 228
<p>1 consistency.</p> <p>2 The consistency in that</p> <p>3 sense, you know, really doesn't surprise</p> <p>4 me. If you take a bunch of studies that</p> <p>5 have the same risk of bias -- and even if</p> <p>6 the level of bias is the same, for</p> <p>7 example, if you're doing a case-control</p> <p>8 study in Boston, I wouldn't expect women</p> <p>9 in Massachusetts to be more prone or less</p> <p>10 prone to recall bias than a group of</p> <p>11 women in California.</p> <p>12 So I wouldn't be surprised</p> <p>13 to see, especially since they are so</p> <p>14 small, similar risk. And that's why I</p> <p>15 have a problem with the commenters in</p> <p>16 Nature to say you don't need these, these</p> <p>17 safe ways, because as long as they keep</p> <p>18 going in the same direction, we should be</p> <p>19 assuming it's real.</p> <p>20 But what if all the studies</p> <p>21 have the same problem, and that problem</p> <p>22 takes your risk estimate in the same</p> <p>23 direction? And that's the problem I have</p> <p>24 with just getting away with intervals,</p>	<p>1 those contained within IARC's or are</p> <p>2 those new studies?</p> <p>3 A. Well, interesting, IARC came</p> <p>4 to the conclusion that it's a possible</p> <p>5 carcinogen --</p> <p>6 Q. Doctor, what was my</p> <p>7 question?</p> <p>8 A. I'm going to answer. And</p> <p>9 this time, you asked me a question, I'm</p> <p>10 going to give you an answer. And --</p> <p>11 Q. Are you going to give me an</p> <p>12 answer that's --</p> <p>13 A. I'm going to give you a very</p> <p>14 direct answer to the question you</p> <p>15 asked --</p> <p>16 Q. That would be great.</p> <p>17 A. -- and if you would give me</p> <p>18 a chance, you would have found out that</p> <p>19 it would have been that case.</p> <p>20 So IARC 2010 looks at talc.</p> <p>21 They have one prospective trial included</p> <p>22 in that.</p> <p>23 In the coming years, you</p> <p>24 asked, are there subsequent data that was</p>
Page 227	Page 229
<p>1 then, in any case.</p> <p>2 So yes, IARC reviewed the</p> <p>3 individual investigator's data and came</p> <p>4 to this conclusion, and they are coming</p> <p>5 to the same conclusion, largely looking</p> <p>6 at the same data.</p> <p>7 Taher's meta-analysis is</p> <p>8 basically Berge's, it's basically</p> <p>9 Penninkilampi. There's no new data in</p> <p>10 there. It's reurning the same data.</p> <p>11 So to say that this is</p> <p>12 consistent with this and this is</p> <p>13 consistent with this, and you're all</p> <p>14 looking at the same studies, to do the</p> <p>15 same thing over and over and expect a</p> <p>16 different outcome is insanity.</p> <p>17 Q. Are you done?</p> <p>18 A. Yes.</p> <p>19 Q. What was my question?</p> <p>20 A. Did I agree with this?</p> <p>21 Q. Okay. That wasn't my</p> <p>22 question.</p> <p>23 The subsequent evaluations</p> <p>24 by individual investigators, are -- are</p>	<p>1 added to it. Well, IARC comes to this</p> <p>2 conclusion, in the subsequent years</p> <p>3 there's three more prospective studies</p> <p>4 that are not included in IARC that come</p> <p>5 to the conclusion that there is no</p> <p>6 association.</p> <p>7 And there are a number of</p> <p>8 pooled analysis, and -- and meta-analysis</p> <p>9 that keeps reurning the same old data</p> <p>10 that's in IARC.</p> <p>11 So there's a number of</p> <p>12 studies that have come out since IARC. I</p> <p>13 would say the balance of which have been</p> <p>14 stronger design studies that have shown</p> <p>15 no increased risk. And I'll be curious</p> <p>16 to see what IARC thinks the next time</p> <p>17 they sit down and pool all this together.</p> <p>18 Q. Doctor, Endnote 3 and 5 and</p> <p>19 69 do not cite to IARC. Are you aware of</p> <p>20 that?</p> <p>21 A. 3, 5 and 69 in IARC?</p> <p>22 Q. Yeah. I'll represent to you</p> <p>23 they're Berge, Penninkilampi and --</p> <p>24 A. Right, so what are Berge and</p>

Kevin Holcomb, M.D.

Page 230	Page 232
<p>1 Penninkilampi, what are the studies in 2 those? 3 Q. Those are just rechurning in 4 your opinion. Those are just -- 5 A. I'm saying -- 6 Q. -- those studies are 7 invaluable because they are just 8 rechurning the prior meta-analyses. 9 Is that your opinion? 10 MS. CURRY: Object to the 11 form. 12 THE WITNESS: I'm saying 13 that there's very little 14 difference between Taher's 15 meta-analysis and Penninkilampi's 16 meta-analysis, and Berge's 17 meta-analysis. 18 The overlap in those studies 19 is great. There's very -- that's 20 not much difference between those. 21 They have very similar number of 22 studies. And so yes, it is a 23 rechurning of the same data. 24 BY MS. GARBER:</p>	<p>1 fact, you'll see that Purdie and Green, 2 same dataset. You'll see that Wu 2015 3 includes Wu 2009. You'll see that Cramer 4 2016 includes Cramer 2009. 5 So is it surprising that 6 2009 Cramer and 2015 Cramer looks the 7 same when the -- half of 2016 is 2009? 8 Q. Shall we throw out -- 9 A. It is rechurning -- 10 Q. Shall we throw out the 11 meta-analysis because they are 12 rechurning? 13 A. I'm saying all -- no. I'm 14 saying that meta -- 15 MS. CURRY: Object to the 16 form. 17 We have to do this in -- in 18 question and answer or you're 19 going to drive the court reporter 20 crazy. 21 THE WITNESS: I apologize. 22 MS. CURRY: Let her get her 23 full question out, give me a 24 second if I need to make an</p>
Page 231	Page 233
<p>1 Q. That doesn't provide you 2 with support that those data are robust? 3 A. If you -- 4 MS. CURRY: Object to the 5 form. 6 THE WITNESS: No. If you -- 7 if you -- 8 BY MS. GARBER: 9 Q. Different authors doing -- 10 picking basically different studies -- 11 A. Different studies? That's 12 what I'm saying, they are not different 13 studies. 14 Q. Okay. 15 A. They're talking the same 16 studies. 17 Q. I'm talking about the body 18 of meta-analyses. 19 A. I'm telling you that 20 Penninkilampi, and Berge, and Taher, if 21 you look at the overlap in the studies 22 that they are putting together, if you 23 look at my case-control list, and it may 24 look like there's so many studies, but in</p>	<p>1 objection, and then please let him 2 finish his answer. 3 BY MS. GARBER: 4 Q. Doctor, should we throw out 5 the meta-analyses because the subsequent 6 meta-analyses are just rechurning of 7 prior meta-analyses? 8 A. No, what I'm saying is don't 9 say Penninkilampi, Berge, and the -- 10 don't count three -- in the same way that 11 in my list of case-control studies, you 12 shouldn't consider Purdie and Green 13 different studies. Even though I have a 14 list there just to show that I was being 15 comprehensive. It's the same dataset. 16 So my point is, if you're 17 look -- if there's a lot of overlap, you 18 shouldn't then look and say, well, this 19 is consistent, because what Bradford Hill 20 meant by consistency was different 21 populations in different places at 22 different times. That's not the spirit 23 of taking the same patients from the same 24 times in the same places and looking at</p>

Kevin Holcomb, M.D.

Page 234	Page 236
<p>1 them over and over again.</p> <p>2 Q. There's not 100 percent</p> <p>3 overlap in any of the studies, is there?</p> <p>4 A. Not 100 percent. But the</p> <p>5 majority of them. The majority of Berge</p> <p>6 is in Taher, and the majority of</p> <p>7 Penninkilampi is in Taher.</p> <p>8 You do the math and tell me</p> <p>9 what percentage is not there. It's the</p> <p>10 same. It's -- the majority, it's the</p> <p>11 same studies.</p> <p>12 Q. In the case-control studies</p> <p>13 is the majority -- are the majority of</p> <p>14 those studies overlap of the prior</p> <p>15 studies?</p> <p>16 MS. CURRY: Object to the</p> <p>17 form.</p> <p>18 THE WITNESS: I don't</p> <p>19 understand what you mean.</p> <p>20 BY MS. GARBER:</p> <p>21 Q. Well, you seem to take issue</p> <p>22 with -- that there's overlap? So</p> <p>23 let's --</p> <p>24 A. There's some.</p>	<p>1 will say that, yes, when you don't have</p> <p>2 overlap you get a 50/50. You get a 50/50</p> <p>3 significance, 50/50 non-significance.</p> <p>4 If you keep churning the</p> <p>5 same data over, you would be surprised to</p> <p>6 see it drop out of significance. And in</p> <p>7 fact, when you look at Berge, which is</p> <p>8 really the only meta-analysis I -- I</p> <p>9 wouldn't say it's the only meta-analysis</p> <p>10 that I respect.</p> <p>11 But one of the rules of</p> <p>12 meta-analysis is that you have to do a</p> <p>13 test for heterogeneity before you just</p> <p>14 decide to throw these studies together</p> <p>15 and it's valid to do so.</p> <p>16 And I look at Penninkilampi.</p> <p>17 And Penninkilampi says, well, I did a</p> <p>18 study for heterogeneity. And I looked</p> <p>19 at, make sure they use condoms and</p> <p>20 diaphragms and perineal dusting. And</p> <p>21 that's what he's looking for</p> <p>22 heterogeneity.</p> <p>23 But the biggest form of</p> <p>24 heterogeneity, the one thing that they</p>
Page 235	Page 237
<p>1 Q. Let's talk about the</p> <p>2 case-control studies.</p> <p>3 A. Sure.</p> <p>4 Q. Do the body of case-control</p> <p>5 studies provide 100 percent overlap of</p> <p>6 data?</p> <p>7 MS. CURRY: Object to the</p> <p>8 form.</p> <p>9 THE WITNESS: No.</p> <p>10 BY MS. GARBER:</p> <p>11 Q. And what's the percentage of</p> <p>12 overlap in your opinion?</p> <p>13 MS. CURRY: Object to the</p> <p>14 form.</p> <p>15 THE WITNESS: I just</p> <p>16 mentioned the studies on my list</p> <p>17 that were overlap.</p> <p>18 BY MS. GARBER:</p> <p>19 Q. Okay. And it's limited to</p> <p>20 those studies, correct?</p> <p>21 A. And you have -- irrespective</p> <p>22 of what the doctors say about throwing</p> <p>23 away confidence intervals, which is not</p> <p>24 the majority of people in medicine, I</p>	<p>1 don't mention, is the first thing Berge</p> <p>2 did. What if you looked at the</p> <p>3 case-control studies and the cohort</p> <p>4 studies? Should these things even be</p> <p>5 mixed together.</p> <p>6 And Berge says, they</p> <p>7 shouldn't. There's too much</p> <p>8 heterogeneity. But they go ahead and do</p> <p>9 it anyway.</p> <p>10 Q. The Penninkilampi authors</p> <p>11 looked at the issue of heterogeneity and</p> <p>12 found --</p> <p>13 A. Through case-control -- I'm</p> <p>14 sorry.</p> <p>15 MS. CURRY: You have to let</p> <p>16 her finish her question.</p> <p>17 THE WITNESS: I'm sorry.</p> <p>18 BY MS. GARBER:</p> <p>19 Q. The Penninkilampi authors</p> <p>20 looked at the issue of heterogeneity and</p> <p>21 concluded that there was not</p> <p>22 heterogeneity with regard to talc</p> <p>23 exposure, true?</p> <p>24 MS. CURRY: Object to the</p>

60 (Pages 234 to 237)

Kevin Holcomb, M.D.

Page 238	Page 240
<p>1 form.</p> <p>2 THE WITNESS: Looking at a</p> <p>3 very similar group of studies as</p> <p>4 Berge, and somehow Berge came up</p> <p>5 with heterogeneity and mentions</p> <p>6 the heterogeneity between study</p> <p>7 design, and Penninkilampi, if you</p> <p>8 look at what they looked at as far</p> <p>9 as heterogeneity, they never say</p> <p>10 that they saw a lack of</p> <p>11 heterogeneity between cohort</p> <p>12 studies and case-control studies.</p> <p>13 And how could you not find</p> <p>14 heterogeneity when you have none</p> <p>15 of the cohort studies showing a</p> <p>16 significant impact?</p> <p>17 BY MS. GARBER:</p> <p>18 Q. Are you an advocate for the</p> <p>19 defense?</p> <p>20 MS. CURRY: Object to the</p> <p>21 form.</p> <p>22 THE WITNESS: I'm an</p> <p>23 advocate for the truth. But I'm</p> <p>24 the biggest advocate for my</p>	<p>1 Q. Very well.</p> <p>2 In the case-control studies</p> <p>3 that are here published in Table 1, do</p> <p>4 those studies involve study participants</p> <p>5 of different ethnicities?</p> <p>6 A. Yes.</p> <p>7 Q. And do those studies involve</p> <p>8 case-control studies that have occurred</p> <p>9 over decades, in other words from 1982 to</p> <p>10 recently?</p> <p>11 A. Yes.</p> <p>12 Q. Okay. And while some of</p> <p>13 them are in the United States, some are</p> <p>14 in foreign countries?</p> <p>15 A. Majority in the United</p> <p>16 States.</p> <p>17 Q. But some are in foreign</p> <p>18 countries?</p> <p>19 A. A few.</p> <p>20 Q. Yeah. And --</p> <p>21 MR. MIZGALA: Could you</p> <p>22 raise your voice just a little</p> <p>23 bit?</p> <p>24 MS. GARBER: Yeah.</p>
Page 239	Page 241
<p>1 patients. But that's a whole</p> <p>2 other story.</p> <p>3 BY MS. GARBER:</p> <p>4 Q. You are an advocate for your</p> <p>5 patients?</p> <p>6 A. I am.</p> <p>7 Q. Do you advise them that it's</p> <p>8 safe to put asbestos on their genitals?</p> <p>9 A. No, I don't.</p> <p>10 MS. CURRY: Is it a good</p> <p>11 time -- good breaking point for</p> <p>12 you?</p> <p>13 MS. GARBER: Sure.</p> <p>14 THE VIDEOGRAPHER: Off the</p> <p>15 record, right? The time is</p> <p>16 1:07 p.m. Off the record.</p> <p>17 (Lunch break.)</p> <p>18 THE VIDEOGRAPHER: We are</p> <p>19 back on the record. The time is</p> <p>20 2:04 p.m.</p> <p>21 BY MS. GARBER:</p> <p>22 Q. Good afternoon, Doctor. Did</p> <p>23 you have a good lunch?</p> <p>24 A. Yes, I did. Thank you.</p>	<p>1 MR. MIZGALA: Thank you.</p> <p>2 BY MS. GARBER:</p> <p>3 Q. And with regard to the</p> <p>4 case-control cohorts and meta-analyses,</p> <p>5 the published literature with regard to</p> <p>6 talc and ovarian cancer contained</p> <p>7 different study designs, can we agree</p> <p>8 with that?</p> <p>9 A. Yes.</p> <p>10 Q. And even within the</p> <p>11 case-control studies, those involve</p> <p>12 different study designs generally?</p> <p>13 MS. CURRY: Object to the</p> <p>14 form.</p> <p>15 THE WITNESS: No. The</p> <p>16 case-control is a study design.</p> <p>17 BY MS. GARBER:</p> <p>18 Q. Okay. I'll just strike</p> <p>19 that.</p> <p>20 All right. Is it your</p> <p>21 opinion that unless a given study is</p> <p>22 statistically significant and with an</p> <p>23 odds ratio greater or equal to 2.0, that</p> <p>24 the findings are attributable to random</p>

61 (Pages 238 to 241)

Kevin Holcomb, M.D.

Page 242	Page 244
<p>1 chance?</p> <p>2 MS. CURRY: Object to the</p> <p>3 form.</p> <p>4 THE WITNESS: No.</p> <p>5 BY MS. GARBER:</p> <p>6 Q. That's not your opinion?</p> <p>7 A. No.</p> <p>8 Q. Who is Melissa Frey?</p> <p>9 A. She is one of my partners at</p> <p>10 Cornell. She is a GYN oncologist.</p> <p>11 Q. Do you respect her as a</p> <p>12 clinician?</p> <p>13 MS. CURRY: Object to the</p> <p>14 form.</p> <p>15 THE WITNESS: Yes, I do.</p> <p>16 BY MS. GARBER:</p> <p>17 Q. Do you respect her</p> <p>18 professional judgment?</p> <p>19 A. Yes.</p> <p>20 Q. You indicate in your expert</p> <p>21 report that use of hormone replacement</p> <p>22 therapy, or can we call that HRT?</p> <p>23 A. It depends what you're</p> <p>24 talking about. If you're talking about a</p>	<p>1 MS. CURRY: Object to the</p> <p>2 form.</p> <p>3 THE WITNESS: Which type of</p> <p>4 cancer are you referring to?</p> <p>5 BY MS. GARBER:</p> <p>6 Q. We'll start with breast</p> <p>7 cancer.</p> <p>8 A. I don't know the odds ratio</p> <p>9 exactly, no.</p> <p>10 Q. Doctor, if I represent to</p> <p>11 you that the odds ratio for Prempro and</p> <p>12 breast cancer is a 1.24, you don't have</p> <p>13 any reason to dispute that, do you?</p> <p>14 MS. CURRY: Object to the</p> <p>15 form.</p> <p>16 THE WITNESS: I -- I don't</p> <p>17 know the odds ratio.</p> <p>18 BY MS. GARBER:</p> <p>19 Q. Do you know, Doctor, or are</p> <p>20 you aware that Prempro carries a black</p> <p>21 box warning for a risk of breast cancer</p> <p>22 based on an odds ratio of 1.24?</p> <p>23 A. For all patients?</p> <p>24 Q. Yes.</p>
Page 243	Page 245
<p>1 combination single -- I -- I assume we're</p> <p>2 going to specify what you're referring</p> <p>3 to.</p> <p>4 Q. Okay. For purposes of your</p> <p>5 expert report with regard to risk factors</p> <p>6 and HRT, what are you referencing?</p> <p>7 A. Most of the studies that</p> <p>8 show a significant increased risk is with</p> <p>9 estrogen replacement alone.</p> <p>10 Q. Okay. And you believe that</p> <p>11 HRT is a risk factor for ovarian cancer,</p> <p>12 or do you limit that to estrogen alone?</p> <p>13 A. I would limit it to estrogen</p> <p>14 alone.</p> <p>15 Q. Okay. In caring for women</p> <p>16 who use HRT in connection with menopause,</p> <p>17 have you had the occasion to prescribe or</p> <p>18 care for a woman using HRT Prempro?</p> <p>19 A. Yes.</p> <p>20 Q. Did you ever prescribe it?</p> <p>21 A. Yes, I have.</p> <p>22 Q. Are you aware that the --</p> <p>23 what the odds ratio or the risks are</p> <p>24 associated with that drug for cancer?</p>	<p>1 A. No, I wasn't aware of that.</p> <p>2 Q. No -- for menopausal women.</p> <p>3 Are you aware of that?</p> <p>4 A. No.</p> <p>5 Q. Do you believe that the risk</p> <p>6 associated with talc and ovarian cancer</p> <p>7 is generally 1.3 to 1.4?</p> <p>8 MS. CURRY: Object to the</p> <p>9 form.</p> <p>10 THE WITNESS: I believe in</p> <p>11 my report I say it's between 1.2</p> <p>12 and 1.6. So I'll stick with that.</p> <p>13 BY MS. GARBER:</p> <p>14 Q. Okay. And so that would be</p> <p>15 a 20 to 60 percent increased risk of</p> <p>16 ovarian cancer associated with talcum</p> <p>17 powder products, right?</p> <p>18 A. In the studies that show a</p> <p>19 risk increase at all, yes.</p> <p>20 Q. And you believe that that</p> <p>21 odds ratio or relative risk is low?</p> <p>22 MS. CURRY: Object to the</p> <p>23 form.</p> <p>24 THE WITNESS: Yes.</p>

Kevin Holcomb, M.D.

Page 246	Page 248
<p>1 BY MS. GARBER: 2 Q. And do you, therefore, feel 3 that it does not meet sufficiency of a 4 magnitude of a risk to be reliable under 5 the Bradford Hill factors? 6 A. No -- 7 MS. CURRY: Object to the 8 form. 9 THE WITNESS: -- that's not 10 my opinion. 11 BY MS. GARBER: 12 Q. Okay. Do you have any 13 opinion as to the magnitude of the risk 14 or strength of the association between 15 the talc literature and ovarian cancer? 16 A. Please repeat the question. 17 Q. Sure. Do you have an 18 opinion as to the strength of the 19 association or magnitude of the risk as 20 it pertains to the talc ovarian cancer 21 literature? 22 MS. CURRY: Object to the 23 form. 24 THE WITNESS: It's generally</p>	<p>1 prevalence is in the United States for 2 use of talcum powder products? 3 MS. CURRY: Object to the 4 form. 5 THE WITNESS: The different 6 studies that I reviewed had 7 different -- different prevalence 8 of use. And I think it's somewhat 9 related to the ethnic group. For 10 example, the group that has 11 probably one of the lowest rates 12 of ovarian cancer is African 13 Americans, and historically they 14 have one of the highest uses of 15 talc. 16 But for example, in Gertig 17 at the -- at that time of that 18 study I believe it was about 19 42 percent of women reported using 20 it with about 14 percent using it 21 daily. 22 BY MS. GARBER: 23 Q. You've seen literature that 24 cites it as high as 50 percent in the</p>
Page 247	Page 249
<p>1 referred to -- it's generally 2 referred to as modest. In some 3 cases weak. And I would -- I 4 would agree with that. 5 BY MS. GARBER: 6 Q. You are aware of 7 peer-reviewed and published studies that 8 hold the opposite opinion to yours, 9 right, that -- that the magnitude of 10 risk -- magnitude of the risk is 11 sufficient to meet with the Bradford Hill 12 criteria as to that issue? 13 A. I agree with the statement 14 that -- I don't agree with the statement 15 that I've seen literature that described 16 the association as anything but modest 17 even in the -- by the authors who hold a 18 different opinion. 19 Q. Do you know what IARC says 20 as to the magnitude of the risk in the 21 2010 monograph? 22 A. I'd have to review it again 23 to say specifically. 24 Q. Do you know what the</p>	<p>1 United States, right? 2 A. Yes. 3 Q. Do you agree with the Narod 4 author in 2016 that it's right to be 5 concerned over carcinogenicity of talc 6 even if a risk ratio is below 50 percent? 7 MS. CURRY: Object to the 8 form. 9 THE WITNESS: No. I think 10 that statement taken in isolation, 11 I would not agree with that. 12 BY MS. GARBER: 13 Q. You agree that his opinion 14 has been published in Gynecologic 15 Oncology, correct? 16 A. I agree, yes. 17 Q. Do you have an opinion as to 18 when subgroup analysis for epithelial 19 ovarian cancer histology type is 20 performed in the studies that serous has 21 the strongest association? 22 MS. CURRY: Object to the 23 form. 24 THE WITNESS: I do. It's</p>

63 (Pages 246 to 249)

Kevin Holcomb, M.D.

Page 250	Page 252
<p>1 not surprising, because it's the</p> <p>2 most predominate cell type.</p> <p>3 BY MS. GARBER:</p> <p>4 Q. Do you agree if women tend</p> <p>5 to use talc daily, as you indicate in</p> <p>6 your report, that the use becomes</p> <p>7 habitual rather than memorable?</p> <p>8 A. Habitual rather than</p> <p>9 memorable?</p> <p>10 Q. Mm-hmm.</p> <p>11 MS. CURRY: Object to the</p> <p>12 form.</p> <p>13 BY MS. GARBER:</p> <p>14 Q. Do you understand the nature</p> <p>15 of my question?</p> <p>16 A. No, I guess I have to think</p> <p>17 about that.</p> <p>18 Q. Let me see if I can help.</p> <p>19 So if, let's say, I have grown up</p> <p>20 brushing my teeth every single day twice</p> <p>21 a day with Crest toothpaste, and somebody</p> <p>22 wants to know what I've done over my</p> <p>23 lifetime, I don't have to think about,</p> <p>24 oh, did I use Crest every single day,</p>	<p>1 including the desirability of the</p> <p>2 exposure.</p> <p>3 But -- so I think all</p> <p>4 behaviors are subject to changes</p> <p>5 in recall based on the specifics.</p> <p>6 BY MS. GARBER:</p> <p>7 Q. Do you believe that the</p> <p>8 case-control studies are unreliable for</p> <p>9 assessment of risk for talcum powder</p> <p>10 exposure in ovarian cancer based on</p> <p>11 recall bias?</p> <p>12 MS. CURRY: Object to the</p> <p>13 form.</p> <p>14 THE WITNESS: I think all</p> <p>15 case-control studies have a risk</p> <p>16 of recall bias, not just limited</p> <p>17 to ovarian cancer studies.</p> <p>18 BY MS. GARBER:</p> <p>19 Q. I understand they're at risk</p> <p>20 for that. Is it your opinion that the</p> <p>21 case-control studies have had recall bias</p> <p>22 at play to explain that increase in risk?</p> <p>23 A. I think that's one of the</p> <p>24 possible explanations, yes.</p>
Page 251	Page 253
<p>1 twice a day? It's habitual because I've</p> <p>2 done it my whole life, rather than if I</p> <p>3 used one product one day and another</p> <p>4 product the other day and, you know, it</p> <p>5 was not something that was part of my</p> <p>6 ADLs. You understand what ADLs are, of</p> <p>7 course.</p> <p>8 A. I do.</p> <p>9 Q. Yeah. Activities of daily</p> <p>10 living. So if it was not part of an</p> <p>11 activity of daily living, it might be</p> <p>12 more memorable.</p> <p>13 Do you understand now?</p> <p>14 MS. CURRY: Object to the</p> <p>15 form.</p> <p>16 THE WITNESS: I -- honestly,</p> <p>17 I think my understanding of this</p> <p>18 isn't that certain things are</p> <p>19 memorable and certain things are</p> <p>20 habitual. It's that activities</p> <p>21 can be impacted by alterations in</p> <p>22 your recall of those things by a</p> <p>23 number of factors, which I</p> <p>24 outlined in my report, one</p>	<p>1 Q. Possible, not probable?</p> <p>2 MS. CURRY: Object to the</p> <p>3 form.</p> <p>4 THE WITNESS: I would argue</p> <p>5 probable.</p> <p>6 BY MS. GARBER:</p> <p>7 Q. Okay. I got you to change</p> <p>8 it to a probable?</p> <p>9 A. Yes.</p> <p>10 Q. Are you aware of literature</p> <p>11 that says it's not likely at play to</p> <p>12 explain the increased odds ratios or</p> <p>13 relative risks?</p> <p>14 A. I have read opinions about</p> <p>15 it, but literature, no.</p> <p>16 Q. Okay. Are you aware of</p> <p>17 authors that have studied the topic of</p> <p>18 talcum powder products and risk of</p> <p>19 ovarian cancer who have concluded that</p> <p>20 recall bias is not at play?</p> <p>21 MS. CURRY: Object to the</p> <p>22 form.</p> <p>23 THE WITNESS: Please repeat</p> <p>24 the question again.</p>

Kevin Holcomb, M.D.

Page 254	Page 256
<p>1 BY MS. GARBER:</p> <p>2 Q. Sure. Have you -- have you</p> <p>3 read peer-reviewed published studies</p> <p>4 where the authors were studying talcum</p> <p>5 powder products and the risk of ovarian</p> <p>6 cancer and have concluded that recall</p> <p>7 bias was not at play as increasing the</p> <p>8 risk for ovarian cancer?</p> <p>9 MS. CURRY: Object to the</p> <p>10 form.</p> <p>11 THE WITNESS: No. In fact,</p> <p>12 the only time I remember a study</p> <p>13 really getting into this where</p> <p>14 they had proof was Schildkraut</p> <p>15 2016, where there was a pretty</p> <p>16 significant increase and people</p> <p>17 remembering being exposed to talc</p> <p>18 after 2014 compared to before</p> <p>19 2014.</p> <p>20 And I can't think of any</p> <p>21 other explanation for that</p> <p>22 difference other than recall bias.</p> <p>23 BY MS. GARBER:</p> <p>24 Q. Well, we'll get to that</p>	<p>1 Here's a screen. The doctor has a</p> <p>2 screen.</p> <p>3 BY MS. GARBER:</p> <p>4 Q. Doctor, at Page 464 of this</p> <p>5 paper, if you can turn to that, the last</p> <p>6 page of the study. And on the left-hand</p> <p>7 column, about halfway down the paragraph,</p> <p>8 it begins "recall."</p> <p>9 Do you see where I am? If</p> <p>10 you look -- if you look here, Doctor.</p> <p>11 See?</p> <p>12 A. Yeah.</p> <p>13 Q. Okay. It reads, "Recall</p> <p>14 bias has also been implicated as a</p> <p>15 limitation in studies of talc and ovarian</p> <p>16 cancer. However, findings in a</p> <p>17 prospective" -- "in a prospective study,</p> <p>18 the Nurses' Health Study, in which</p> <p>19 exposure data were collected prior to</p> <p>20 diagnosis and hence free of recall bias</p> <p>21 were similar to the present finding for</p> <p>22 our talc use and serous invasive ovarian</p> <p>23 cancer.</p> <p>24 "It has also been suggested</p>
Page 255	Page 257
<p>1 paper. And I appreciate that. But you</p> <p>2 just used a term, "proof." What do you</p> <p>3 mean by that?</p> <p>4 A. I don't know exactly what I</p> <p>5 said. Can you repeat my statement?</p> <p>6 Q. You said, "I remember a</p> <p>7 study really getting into this where they</p> <p>8 had proof, was Schildkraut 2016, where</p> <p>9 there were pretty significant" --</p> <p>10 A. Let me change the word from</p> <p>11 "proof" to "evidence."</p> <p>12 Q. Okay. Let's look at some</p> <p>13 studies.</p> <p>14 (Document marked for</p> <p>15 identification as Exhibit</p> <p>16 Holcomb-13.)</p> <p>17 BY MS. GARBER:</p> <p>18 Q. I'm going to mark as</p> <p>19 Exhibit 13 a paper by Mills, et al. This</p> <p>20 is one that you reviewed, right?</p> <p>21 A. Yes.</p> <p>22 MS. GARBER: Sorry. I</p> <p>23 didn't -- I didn't make enough</p> <p>24 copies for you guys. I apologize.</p>	<p>1 that use of talc is habitual versus</p> <p>2 memorable and not likely to be subject to</p> <p>3 recall bias."</p> <p>4 So, Doctor, my question is,</p> <p>5 this is a peer-reviewed study author who</p> <p>6 is suggesting that the studies are</p> <p>7 similar between case-control and a cohort</p> <p>8 and suggesting that recall bias is not at</p> <p>9 play because the use is habitual versus</p> <p>10 memorable.</p> <p>11 Do you agree?</p> <p>12 MS. CURRY: Object to the</p> <p>13 form.</p> <p>14 THE WITNESS: No. Can I</p> <p>15 explain why?</p> <p>16 BY MS. GARBER:</p> <p>17 Q. I don't -- I don't mean</p> <p>18 agree with the author. Do you agree with</p> <p>19 my assessment of what the authors are</p> <p>20 saying?</p> <p>21 MS. CURRY: Object to the</p> <p>22 form.</p> <p>23 THE WITNESS: That's true</p> <p>24 what the authors are saying.</p>

65 (Pages 254 to 257)

Kevin Holcomb, M.D.

Page 258	Page 260
<p>1 BY MS. GARBER: 2 Q. Okay. And you disagree that 3 recall bias is not at play because the 4 use is habitual rather than memorable? 5 A. No. 6 Q. You don't agree with that? 7 A. If I can explain my 8 reasoning, or should I leave this at yes 9 or no? 10 Q. Just I don't need to know 11 why. 12 A. You don't need to know why. 13 Q. No, I want to ask you a few 14 more questions and then I'll circle back 15 to that -- 16 A. Sure. 17 Q. -- because there are a few 18 other papers that I want to get to before 19 we understand that. 20 Doctor, if you can go back 21 to the Health Canada, which we marked as 22 Exhibit 11. And if you could turn to 23 Page 28. Under -- do you see where I am? 24 Under the 6.4, third paragraph down.</p>	<p>1 form. 2 THE WITNESS: One, the first 3 statement, "The recall bias is 4 unlikely to be an important source 5 of bias," is now referring to an 6 opinion of Narod. Narod's 2016, I 7 told you was that not -- that 8 wasn't based on data. So there's 9 an echo chamber thing. 10 And then the positive 11 association is strongest for 12 serous histologic type, if you 13 have a higher prevalence of a 14 type, you would expect recall bias 15 to be more commonly seen with 16 that, because when you have rarer, 17 smaller numbers, you may not reach 18 an association high enough to show 19 the increased risk there. 20 So it's not surprising to me 21 if there was going to be a 22 consistent cell type that you saw 23 this increased risk with, it would 24 be with serous, because it is the</p>
Page 259	Page 261
<p>1 Do you see where I am? It 2 says, "In studies?" 3 A. 28. Yes. Yes. Okay. 4 Q. It says, "In studies where 5 the exposure is simple, e.g., never 6 versus ever use, recall bias is unlikely 7 to be an important source of bias." And 8 then it cites to Narod 2016. 9 "The positive association is 10 strongest for serous histologic type," 11 and then it cites to Berge 2018 and Taher 12 2018. "Findings that the association may 13 vary by histologic type detracts from the 14 hypothesis of report bias as this type of 15 bias would likely operate for all 16 histologic types." 17 Did I read that correctly? 18 A. You did. 19 Q. And so what the authors 20 there are saying is if recall bias was at 21 play here, you would expect to see an 22 increase in all of the histologic types, 23 not just certain ones, correct? 24 MS. CURRY: Object to the</p>	<p>1 predominate cell type. 2 BY MS. GARBER: 3 Q. You disagree with the study 4 authors of Health Canada wherein they are 5 stating at Page 28, that recall bias is 6 not likely at play -- 7 A. They are -- yeah, I'm sorry. 8 Q. -- not likely at play for 9 the increased risk amongst the studies, 10 correct? 11 A. I do because if they would 12 cite a study where they can show it 13 wasn't at play. See, I can cite a study 14 where I believe it was at play when I 15 cite Schildkraut. 16 When they cite a study that 17 shows it's not at play, they cite an 18 opinion piece by Narod. There's a 19 difference. 20 Q. Well, and they also cite the 21 Berge and Taher papers, don't they? 22 A. For a different period -- 23 for a different point. 24 Q. Is there any metric,</p>

66 (Pages 258 to 261)

Kevin Holcomb, M.D.

Page 262	Page 264
<p>1 objective metric to measure recall bias 2 in a given study? In other words, for 3 those who don't typically read 4 epidemiological literature, there -- 5 there is not an objective measurement 6 that can be -- 7 A. I can think of one. 8 MS. CURRY: Object to the 9 form. 10 THE WITNESS: If you have a 11 situation where there is a -- an 12 increase in familiarity with a 13 topic that happens after a certain 14 time point and you look at the 15 association before and after this 16 is widely known and show that 17 there's a difference, I think that 18 that's a fair metric -- it puts 19 the onus to figure out, well, why 20 all of a sudden after the time 21 that it's a well-known entity, why 22 do more people remember using it 23 who have cancer compared to the 24 controls.</p>	<p>1 isn't it? I mean, how does a study 2 author decide what is and what isn't 3 likely known? 4 A. Well, if you -- I think it's 5 a fair thing to ask. But if you have a 6 date where there's a big lawsuit, per 7 se -- per se. And I bet you if you 8 counted how many commercials you see on a 9 topic, a liability topic, I bet you can 10 come up with a clear point where you can 11 say before this time frame there was this 12 amount of activity on TV, and after this 13 time frame, it was that much. And -- and 14 yeah, that was a crude estimate to do it 15 with what date the -- the first cases are 16 becoming very well known. 17 But I disagree with the 18 point that you can't approximate recall 19 bias. Because I -- I do think 20 Schildkraut's study was a good example of 21 it. 22 Q. The Schildkraut separated 23 the -- what was known from what was not 24 known based on a time frame of 2014,</p>
Page 263	Page 265
<p>1 So if the controls have the 2 same memory of using it before 3 it's widely known as after it's 4 widely known, but the cases, all 5 of the sudden after it's widely 6 known the cases remember using, 7 this habitual practice, all of the 8 sudden goes up, after it's widely 9 known, I take that as a fair 10 metric of recall bias. 11 And I've tried to explain in 12 my mind what other thing could get 13 played to explain that finding, 14 and I can't. 15 So with all due respect to 16 Dr. Narod's opinion, which is not 17 citing a paper, I have seen data 18 where I think -- I can't think of 19 another plausible explanation for 20 what's at play other than recall 21 bias using the metric I just 22 described. 23 BY MS. GARBER: 24 Q. Widely known is subjective,</p>	<p>1 correct? 2 A. Right. 3 Q. And what was known, what was 4 widely known in 2014 in your opinion? 5 MS. CURRY: Object to the 6 form. 7 THE WITNESS: Well, I don't 8 think it was as widely known 9 before 2014 of large payments and 10 lawsuits because of talc being 11 associated with -- with ovarian 12 cancer. 13 Because it's my assumption 14 that most lay people don't know of 15 the association because they've 16 been reading Cramer studies, or 17 Merritt or any of these other -- 18 I'm -- I'm going to assume that 19 the majority of people out there 20 who are going to be on these 21 studies and answering these 22 questionnaires, how are they going 23 to find out about talc. It's most 24 likely going to come through the</p>

67 (Pages 262 to 265)

Kevin Holcomb, M.D.

Page 266	Page 268
<p>1 lay media.</p> <p>2 The lay media pipes up more</p> <p>3 when there is product liability</p> <p>4 associated with it.</p> <p>5 BY MS. GARBER:</p> <p>6 Q. When --</p> <p>7 A. And so --</p> <p>8 Q. When was that first time</p> <p>9 that there was lay media coverage of a</p> <p>10 talc verdict or litigation?</p> <p>11 A. I don't think it's -- I</p> <p>12 can't give you the exact date where it</p> <p>13 starts. I think you'd have to look, and</p> <p>14 split your studies up into an earlier</p> <p>15 period and a later period.</p> <p>16 But, if people who don't</p> <p>17 have ovarian cancer have the same</p> <p>18 recollection of talc usage before and</p> <p>19 after a certain point, but cases have a</p> <p>20 very different memory of using it before</p> <p>21 and after, I think that that's a very,</p> <p>22 very powerful statement, and I would</p> <p>23 argue that you'd be challenged to come up</p> <p>24 with another reason why that would</p>	<p>1 describing.</p> <p>2 I believe it was at play in</p> <p>3 Schildkraut. And I don't believe</p> <p>4 there is anything special about</p> <p>5 Schildkraut's study design that</p> <p>6 would make it at play in that</p> <p>7 study and not another one.</p> <p>8 BY MS. GARBER:</p> <p>9 Q. Okay. Your opinion that</p> <p>10 there's recall bias at play in the</p> <p>11 case-control studies is based on</p> <p>12 Schildkraut's study?</p> <p>13 MS. CURRY: Object to the</p> <p>14 form.</p> <p>15 THE WITNESS: Not only.</p> <p>16 BY MS. GARBER:</p> <p>17 Q. What -- what other data do</p> <p>18 you have to support that claim?</p> <p>19 A. A trend in the strength of</p> <p>20 association also increasing over time.</p> <p>21 Q. Is that your opinion?</p> <p>22 A. Yes.</p> <p>23 Q. That there is a trend of</p> <p>24 increasing --</p>
Page 267	Page 269
<p>1 happen, other than recall bias.</p> <p>2 Q. Are you aware of</p> <p>3 peer-reviewed study authors that state in</p> <p>4 their papers with regard to talcum powder</p> <p>5 product use and ovarian cancer, that say</p> <p>6 reporting bias is not at play with regard</p> <p>7 to the results?</p> <p>8 MS. CURRY: Object to the</p> <p>9 form.</p> <p>10 THE WITNESS: I'm not</p> <p>11 familiar with, and you -- you</p> <p>12 posited that there's no good</p> <p>13 metric. So I'm not sure, other</p> <p>14 than me describing examples where</p> <p>15 I believe it's at play and</p> <p>16 explaining why, I would be curious</p> <p>17 to hear the opinion of somebody</p> <p>18 like Narod who says I don't</p> <p>19 believe it's at play.</p> <p>20 And if your only</p> <p>21 justification for the statement is</p> <p>22 that I believe it's habitual</p> <p>23 versus memorable, that is less</p> <p>24 persuasive than what I'm</p>	<p>1 A. To be fair the term</p> <p>2 "trend" --</p> <p>3 Q. -- risk over time?</p> <p>4 A. I'm sorry.</p> <p>5 Q. Sorry.</p> <p>6 A. The term "trend" is a -- is</p> <p>7 a statistical term. So I -- I can't say</p> <p>8 I've subjected this to a statistical</p> <p>9 test.</p> <p>10 But in earlier versus later</p> <p>11 studies, you do see an increase.</p> <p>12 Q. And, Doctor, if we look at</p> <p>13 your Table 1 and we look at the odds</p> <p>14 ratios -- or sorry, the relative risk,</p> <p>15 do --</p> <p>16 A. Let me go back.</p> <p>17 Q. -- does it show an increase</p> <p>18 over time?</p> <p>19 A. Let me go back one second.</p> <p>20 Q. It's Exhibit 9.</p> <p>21 A. I'd have to take the time to</p> <p>22 look through all the odds ratios, but one</p> <p>23 of the reasons why I color-coded it was I</p> <p>24 can just look at that and -- and see that</p>

68 (Pages 266 to 269)

Kevin Holcomb, M.D.

Page 270	Page 272
<p>1 there's more blue which are 2 nonsignificant studies -- 3 Q. Well -- 4 A. -- in the beginning -- 5 Q. Well, Doctor -- 6 A. -- and these -- these are 7 in -- in chronological order. 8 Q. Let's just look at the -- at 9 the white ones. 10 The odds ratios don't seem 11 to be increasing over time appreciably, 12 do they? 13 A. Not to my naked eye, no. 14 Q. Okay. 15 A. Just the frequency of 16 positive studies. 17 Q. And we're going to get to 18 the meta-analysis shortly. But the 19 meta-analyses over time. How many 20 meta-analyses are there, by the way? 21 A. There's probably about 22 seven. Maybe more. 23 Q. And do you, off the top of 24 your head, do you have a general sense of</p>	<p>1 case-control studies. It could have been 2 a problem had there been widespread 3 publicity about the possible association 4 between use of body powder and cancer. 5 The IARC" -- shortened that -- "working 6 group considers that there has not been 7 widespread public concern about the issue 8 and, therefore, considers it unlikely 9 that such a bias could explain the 10 consistent findings." 11 Did I read that correctly? 12 A. You did. And you're talking 13 about one type of recall bias. The 14 authors go on to say that's not the only 15 type of recall bias that we have to 16 consider. And in fact just recall bias 17 in cancer patients remembering exposures 18 at a higher rate cannot be ruled out. 19 Q. Doctor, you can't say to a 20 medical degree of probability that there 21 is recall bias that explain the 22 statistically significant increased risk 23 in the case-control studies, can you? 24 MS. CURRY: Object to the</p>
Page 271	Page 273
<p>1 what those odds ratios are? 2 A. Yes. I believe they're in 3 the same modest range as the studies that 4 are going into them. 1.24, 1.28, 1.31, 5 in that general region. 6 Q. Let's look at another paper, 7 the Langseth paper. You reviewed that as 8 part of your expert opinions, right? 9 A. Yes. 10 (Document marked for 11 identification as Exhibit 12 Holcomb-14.) 13 BY MS. GARBER: 14 Q. And if you turn to page -- 15 well, it's 358. It's the front page, 16 Doctor. 17 And if you look at -- if you 18 look at the right-hand column about 19 halfway down -- do you see where I am? 20 Where it says, "Methodological factors"? 21 A. Yes, I do. 22 Q. And the paper reads, 23 "Methodological factors such as recall 24 bias should always be considered in</p>	<p>1 form. 2 THE WITNESS: No. 3 BY MS. GARBER: 4 Q. In your expert report, do 5 you address at all anywhere in the four 6 corners of your report where study 7 authors -- peer-reviewed study authors 8 have indicated that recall bias is not 9 likely at play to explain the increased 10 risk? Do you address that issue at all? 11 A. No. 12 Q. And anywhere in the four 13 corners of your report, do you address 14 that study authors, peer-reviewed study 15 authors, have indicated that the 16 epidemiological data is consistent? 17 A. Do I present the data in my 18 report showing a 50/50 split and then say 19 that other people called it consistent? 20 No, I didn't. 21 Q. Let's turn to the 22 Schildkraut paper. 23 (Document marked for 24 identification as Exhibit</p>

Kevin Holcomb, M.D.

<p style="text-align: right;">Page 274</p> <p>1 Holcomb-15.)</p> <p>2 BY MS. GARBER:</p> <p>3 Q. I'm going to mark it as 15.</p> <p>4 Doctor, in your expert report at Page 9,</p> <p>5 you indicate that, "Recall bias can lead</p> <p>6 to spurious results in case-control</p> <p>7 studies in a variety" --</p> <p>8 A. I'm sorry. Which page were</p> <p>9 you reading from?</p> <p>10 Q. Page 9. You indicate that,</p> <p>11 "Recall bias can lead to spurious results</p> <p>12 in case-control studies in a variety</p> <p>13 of" --</p> <p>14 A. I'm sorry. I'm still trying</p> <p>15 to find out where we are. I don't</p> <p>16 think --</p> <p>17 Q. I'm just --</p> <p>18 A. One second.</p> <p>19 Q. I'm just reading.</p> <p>20 A. I know. I just want to read</p> <p>21 along, if it's okay.</p> <p>22 Yes, I'm ready for you.</p> <p>23 Q. I'll try it again. You</p> <p>24 indicate that, "Recall bias can lead to</p>	<p style="text-align: right;">Page 276</p> <p>1 once.</p> <p>2 MS. CURRY: Where are you?</p> <p>3 MS. GARBER: Right here.</p> <p>4 THE WITNESS: Yes, I found</p> <p>5 it.</p> <p>6 BY MS. GARBER:</p> <p>7 Q. "Although our findings</p> <p>8 suggest that the publicity of class</p> <p>9 action lawsuits may have resulted in</p> <p>10 increased reporting of body powder use,</p> <p>11 our data do not support that recall bias</p> <p>12 alone before 2014 versus" -- "before 2014</p> <p>13 versus 2014 or later would account for</p> <p>14 the associations with body powder use and</p> <p>15 epithelial ovarian cancer."</p> <p>16 Did I read that correctly?</p> <p>17 A. Yes, you did.</p> <p>18 Q. So you didn't cite that in</p> <p>19 your expert report, did you?</p> <p>20 A. I -- maybe I'm</p> <p>21 misunderstanding what they are saying</p> <p>22 here. But they're saying maybe it's not</p> <p>23 just not that alone. They're saying that</p> <p>24 there could be other things that cause</p>
<p style="text-align: right;">Page 275</p> <p>1 spurious results in case-control studies</p> <p>2 in a variety of clinical scenarios." And</p> <p>3 then you cite to the Schildkraut 2016</p> <p>4 paper, correct?</p> <p>5 A. Right.</p> <p>6 Q. All right. And --</p> <p>7 A. Hold on. Is that</p> <p>8 Schildkraut that I'm -- let me see. 33,</p> <p>9 yes.</p> <p>10 Q. What you didn't cite to is</p> <p>11 that the -- is what the authors stated</p> <p>12 about the class action publicity. And so</p> <p>13 if I can have you turn to Page 1416 of</p> <p>14 the Schildkraut paper.</p> <p>15 And so if you go to the</p> <p>16 right-hand column, in the first paragraph</p> <p>17 about halfway down with the sentence that</p> <p>18 begins "although."</p> <p>19 Do you see where I am?</p> <p>20 A. Yes.</p> <p>21 Q. It says, "Although our</p> <p>22 findings" --</p> <p>23 A. No. I'm sorry. Wrong</p> <p>24 although. They say "although" more than</p>	<p style="text-align: right;">Page 277</p> <p>1 recall bias. And they're saying --</p> <p>2 they're not discounting that that played</p> <p>3 a role. They're saying there could be</p> <p>4 other things, and they are pretty much</p> <p>5 saying the same thing that I read before</p> <p>6 where they said there's other causes of</p> <p>7 recall bias other than just information</p> <p>8 out in the media.</p> <p>9 Possibly there were multiple</p> <p>10 things at play that caused recall bias.</p> <p>11 But that statement, they're not saying</p> <p>12 there was no recall bias in the study.</p> <p>13 They're just saying that it may be more</p> <p>14 than just -- than just the lawsuits.</p> <p>15 Q. That's your interpretation</p> <p>16 of what they are saying?</p> <p>17 A. Well, it says --</p> <p>18 MS. CURRY: Object to the</p> <p>19 form.</p> <p>20 THE WITNESS: -- it says,</p> <p>21 "The data do not support the</p> <p>22 recall bias alone before 2014</p> <p>23 versus" -- "or later would account</p> <p>24 for the associations." They</p>

70 (Pages 274 to 277)

Kevin Holcomb, M.D.

Page 278	Page 280
<p>1 didn't say that it didn't. 2 They're just saying possibly 3 there's other things. 4 Yes, that's my 5 interpretation. 6 BY MS. GARBER: 7 Q. You don't know what the 8 other things are, do you? 9 A. They don't either. They're 10 saying -- they're not discounting recall 11 bias. They're just saying there may be 12 multiple sources. 13 Q. There was no widespread 14 publicity about talc and ovarian cancer 15 in the lay media in 2014, was there? 16 MS. CURRY: Object to the 17 form. 18 THE WITNESS: Then why did 19 Schildkraut decide to make that 20 analysis? They made that analysis 21 specifically because of the 22 lawsuits. 23 BY MS. GARBER: 24 Q. You're making that</p>	<p>1 They then design an experiment to see if 2 they could show a difference, and guess 3 what? The findings show exactly that. 4 That controls have the same level of 5 memory of exposure but the cases all of 6 the sudden jump up after 2014. 7 If you do an experiment 8 because you have a hypothesis, and your 9 experiment then proves the hypothesis, 10 you should reasonably say, this is why I 11 did it. I found what I found. I have 12 evidence of recall bias. That's the 13 whole point why they did this experiment. 14 Q. Did the Schildkraut authors 15 find a statistically significant finding 16 between genital powder use and epithelial 17 ovarian cancer? 18 A. Yes. What I found 19 interesting about -- 20 Q. Doctor, I didn't -- 21 A. I won't editorialize. I 22 won't -- sorry. 23 Q. I appreciate that. 24 A. Sure.</p>
Page 279	Page 281
<p>1 assumption, aren't you? 2 MS. CURRY: Object to the 3 form. 4 THE WITNESS: No. They -- 5 they say in the materials and 6 methods, why they split at 2014. 7 BY MS. GARBER: 8 Q. Do you know -- 9 A. They didn't just routinely 10 pick that up. 11 Q. I understand that, Doctor. 12 A. Right. 13 Q. But authors can make 14 mistakes, can't they? 15 A. I've been pointing out a lot 16 of them. 17 Q. Okay. You didn't point out 18 this one, did you? 19 A. Which mistake? 20 Q. Well, do you know if there 21 was widespread publicity about lawsuits 22 in 2014? 23 A. The authors consider that 24 maybe publicity would make a difference.</p>	<p>1 Q. At Page 8, Figure 1 of your 2 expert report, if we can turn there. 3 Are you there? 4 A. I am. 5 Q. Here you have a diagram 6 regarding the levels of evidence; is that 7 right? 8 A. Yes. 9 Q. I'll publish it on the Elmo. 10 This is your diagram for the levels of 11 evidence, correct? 12 A. It's not my diagram. 13 Q. In fact, it's the levels of 14 evidence for the Center For 15 Evidence-Based Medicine, or the CEBMA, 16 correct? 17 A. Management, yes. 18 Q. And what -- is that a 19 medical site or is that a business site? 20 A. I'm not sure. 21 Q. Why did you pick that 22 diagram? 23 A. I was looking -- I was 24 looking for an example of the -- what I</p>

71 (Pages 278 to 281)

Kevin Holcomb, M.D.

Page 282	Page 284
<p>1 believe is a widely held hierarchy on the</p> <p>2 strengths of different study types based</p> <p>3 on their ability to be altered by</p> <p>4 inaccuracies. And this was the diagram</p> <p>5 that I found that I thought showed it the</p> <p>6 best.</p> <p>7 Q. Did you just look to find a</p> <p>8 diagram where cohorts were above</p> <p>9 case-control studies, is that how you</p> <p>10 searched?</p> <p>11 MS. CURRY: Object -- object</p> <p>12 to the form.</p> <p>13 THE WITNESS: If you search</p> <p>14 under levels of evidence, you will</p> <p>15 never find -- well, I may not say</p> <p>16 never. Who knows.</p> <p>17 I -- I don't think you</p> <p>18 will -- you have to search hard to</p> <p>19 find a -- a figure that has cohort</p> <p>20 studies above case-control</p> <p>21 studies.</p> <p>22 BY MS. GARBER:</p> <p>23 Q. Okay. So what you said is</p> <p>24 if you search under levels of evidence,</p>	<p>1 this.</p> <p>2 This is how I was -- this is</p> <p>3 how I was trained. I mean, this -- I'm</p> <p>4 looking for -- there are some things that</p> <p>5 I learned in reviewing for the -- for</p> <p>6 this deposition. And there are certain</p> <p>7 beliefs that I've long held because I was</p> <p>8 trained that way. I was forced -- well,</p> <p>9 not forced. I was happily taking a</p> <p>10 graduate level statistics course as part</p> <p>11 of my fellowship. And I was taught this</p> <p>12 then too. And that was part of a medical</p> <p>13 statistics course.</p> <p>14 So this is just consistent</p> <p>15 with what I already knew.</p> <p>16 Q. Where do meta-analyses fall</p> <p>17 on your pyramid?</p> <p>18 A. You know, the reason why</p> <p>19 meta-analyses aren't on these is because</p> <p>20 meta-analysis is a somewhat controversial</p> <p>21 practice. They -- there are some</p> <p>22 strengths to meta-analysis. There are</p> <p>23 some ways that meta-analyses can help.</p> <p>24 But you have to really, really conduct</p>
Page 283	Page 285
<p>1 you will never find -- I mean -- I mean I</p> <p>2 may not say never. Who knows. You have</p> <p>3 to search hard to find a figure that has</p> <p>4 cohorts above case-control studies.</p> <p>5 Is that your testimony?</p> <p>6 A. I'm sorry. It's below.</p> <p>7 Sorry. The other way around. Thank you.</p> <p>8 Q. Thanks for that.</p> <p>9 Did you attempt to find a</p> <p>10 medical website or an evidence-based</p> <p>11 medical website as to the levels of</p> <p>12 evidence?</p> <p>13 MS. CURRY: Object to the</p> <p>14 form.</p> <p>15 BY MS. GARBER:</p> <p>16 Q. Or did you find this one and</p> <p>17 stop?</p> <p>18 A. I -- I don't -- I don't</p> <p>19 think that whether -- statistics don't</p> <p>20 alter from one practice to the other.</p> <p>21 Weaknesses in a study design are built in</p> <p>22 and baked in. And so no, I didn't look</p> <p>23 for a specific medical website, because I</p> <p>24 thought it would look differently than</p>	<p>1 them in a strict format and not break the</p> <p>2 rules. So you can have a meta-analysis</p> <p>3 that's well -- you know, very well</p> <p>4 controlled, and look for heterogeneity</p> <p>5 and did all the things that you have to</p> <p>6 do, that would be a strong study. But</p> <p>7 it's so fraught with the ability to make</p> <p>8 it a poor study. So it's hard to put it</p> <p>9 on here. Because there is no one</p> <p>10 meta-analysis that's going to be</p> <p>11 positive. It's going to be a good study.</p> <p>12 Q. What -- what is your basis</p> <p>13 to say that -- that meta-analyses are</p> <p>14 controversial?</p> <p>15 A. Let me go through. I -- I</p> <p>16 thought I had actually given a citation</p> <p>17 for it when I said -- because I believe I</p> <p>18 made that statement in here as well.</p> <p>19 You know, I didn't cite to</p> <p>20 a -- to an exact paper.</p> <p>21 Q. So that's the opinion of</p> <p>22 Dr. Holcomb --</p> <p>23 A. No, I wish I had cited it,</p> <p>24 because I actually reviewed different</p>

72 (Pages 282 to 285)

Kevin Holcomb, M.D.

Page 286	Page 288
<p>1 study designs. Not just for this. And</p> <p>2 that is, if given the -- the time, I</p> <p>3 could find a citation that makes the same</p> <p>4 statement. It's not just my opinion.</p> <p>5 Q. But there's not one in your</p> <p>6 report?</p> <p>7 A. There's not one in my</p> <p>8 report, no.</p> <p>9 Q. You can't think of one</p> <p>10 either, can you?</p> <p>11 A. No, I would have to do a</p> <p>12 search.</p> <p>13 Q. So when you had your</p> <p>14 statistics class, what was your text, do</p> <p>15 you remember?</p> <p>16 MS. CURRY: Object to the</p> <p>17 form.</p> <p>18 THE WITNESS: I don't.</p> <p>19 BY MS. GARBER:</p> <p>20 Q. And I asked you this before,</p> <p>21 if you knew who Kenneth Rothman was in</p> <p>22 the context of epidemiology. And you did</p> <p>23 not, correct?</p> <p>24 A. That's correct.</p>	<p>1 form.</p> <p>2 THE WITNESS: No. As I</p> <p>3 stated before, I would have to</p> <p>4 search and find you one.</p> <p>5 BY MS. GARBER:</p> <p>6 Q. Did you know that Kenneth</p> <p>7 Rothman is known for his work on teaching</p> <p>8 about epidemiologic research methodology?</p> <p>9 MS. CURRY: Object to the</p> <p>10 form.</p> <p>11 BY MS. GARBER:</p> <p>12 Q. Were you aware of that?</p> <p>13 A. Given the fact that I --</p> <p>14 I've already answered that I wasn't aware</p> <p>15 who he is, I don't see how I would know</p> <p>16 that.</p> <p>17 Q. Do you ever rely on</p> <p>18 meta-analyses in your practice to make</p> <p>19 clinical decisions, do you ever look at</p> <p>20 epidemiological data and set your care</p> <p>21 attendant to the results or are they just</p> <p>22 worthwhile in your opinion?</p> <p>23 MS. CURRY: Object to the</p> <p>24 form.</p>
Page 287	Page 289
<p>1 Q. So I'll represent to you</p> <p>2 that he is a professor of epidemiology,</p> <p>3 an author of textbooks and many published</p> <p>4 articles regarding epidemiology. Okay?</p> <p>5 I'll also show you that he</p> <p>6 is the study author of this widely used</p> <p>7 text with regard to epidemiology. You</p> <p>8 see that Kenneth Rothman is the first</p> <p>9 author, Sander Greenland is the second.</p> <p>10 And that goes back to that paper on</p> <p>11 statistical significance. That's the</p> <p>12 author, right?</p> <p>13 You are not familiar with</p> <p>14 those authors or this text; is that</p> <p>15 correct?</p> <p>16 A. Or the fact that it's widely</p> <p>17 used, no.</p> <p>18 Q. Okay. You've never read a</p> <p>19 book with regard to meta-analyses and the</p> <p>20 utility of them -- strike that.</p> <p>21 Can you name a text with</p> <p>22 regard to meta-analyses and the utility</p> <p>23 of them?</p> <p>24 MS. CURRY: Object to the</p>	<p>1 THE WITNESS: No, no,</p> <p>2 they're worthwhile but they -- we</p> <p>3 don't -- I've never made any</p> <p>4 clinical decisions on care based</p> <p>5 on one study. It's -- it's --</p> <p>6 meta-analysis will become part of</p> <p>7 the totality of what I'm looking</p> <p>8 at.</p> <p>9 BY MS. GARBER:</p> <p>10 Q. Meta-analysis is looking at</p> <p>11 a systematic review of a body of</p> <p>12 literature, correct?</p> <p>13 A. Meta-analysis is taking</p> <p>14 subjects that were in different places</p> <p>15 and different times and mixing them up as</p> <p>16 if they were all in the same place at the</p> <p>17 same time under the same conditions,</p> <p>18 hence it's fraught with potential issues.</p> <p>19 Q. There's utility to them,</p> <p>20 isn't there?</p> <p>21 MS. CURRY: Object to the</p> <p>22 form.</p> <p>23 THE WITNESS: If done</p> <p>24 correctly, yes.</p>

73 (Pages 286 to 289)

Kevin Holcomb, M.D.

Page 290	Page 292
<p>1 BY MS. GARBER: 2 Q. What are -- what is the 3 utility of them? 4 A. For example, if you had -- 5 this question of do you have enough 6 numbers in your cohort studies to 7 approximate an effect size that you see 8 in your case-control studies, well, you 9 might be able to do that in a 10 meta-analysis. You might be able to put 11 all these things together. 12 And Berge says when we put 13 everything together, we felt we had 14 99 percent chance of finding the effect 15 size in the case-control size when we put 16 all the people together from the three 17 cohort studies that Berge put together. 18 So that's an example where 19 it might be helpful. If you think you 20 can put together studies that are biased 21 for example, and that if you mix them 22 altogether the bias will be diluted, 23 that's where it's not helpful. 24 Q. Do you have a source to cite</p>	<p>1 the bias? I don't can't think of a 2 source. I know it's not -- I know even 3 some of your experts don't -- don't 4 refute that. Ellen Blair Smith says as 5 much in her -- in her expert report. She 6 agrees that that's the case. 7 Q. Does she say there's no 8 utility to the meta-analyses because of 9 bias? 10 A. I didn't -- I didn't say 11 that. If you're asking me about the 12 statement, I can tell you that I can find 13 support of that statement by some of the 14 plaintiff experts. 15 Q. Let's look at a paper by Ken 16 Rothman. 17 (Document marked for 18 identification as Exhibit 19 Holcomb-16.) 20 BY MS. GARBER: 21 Q. I'm going to mark as 22 Exhibit 16 a paper titled "Six Persistent 23 Research Misconceptions" by Kenneth 24 Rothman. You've not seen that paper</p>
Page 291	Page 293
<p>1 that when you put cohort studies 2 together, that the bias will affect the 3 results of a meta-analysis? 4 MS. CURRY: Object to the 5 form. 6 THE WITNESS: I didn't -- 7 that wasn't my statement. 8 BY MS. GARBER: 9 Q. Do you have a source for 10 that? 11 A. I didn't say that. So why 12 would I have a source? 13 Q. Do you have a source for 14 what you just said? 15 A. Please repeat it. 16 Q. You said, "If you think you 17 can put together studies that are biased, 18 for example, and that if you mix them 19 together, although the bias will be 20 diluted, that's where it's not helpful." 21 What is your source for that 22 statement? 23 A. The source? That adding 24 biased studies together doesn't dilute</p>	<p>1 before? 2 A. No. 3 Q. Doctor, if you look at the 4 left-hand column, do you see here that's 5 illuminated or highlighted? 6 Do you see where I am? 7 A. Yes, I do. 8 Q. It reads, "Scientific 9 knowledge changes rapidly, but the 10 concepts and methods of conduct of 11 research change more slowly. To 12 stimulate discussion of outmoded thinking 13 regarding the conduct of research, I list 14 six misconceptions about research that 15 persist long after their flaws become 16 apparent. 17 "These misconceptions are: 18 "Number one, the 19 hierarchy" -- I'm sorry. 20 "Number one, there is a 21 hierarchy of study designs. Randomized 22 trials provide the greatest validity 23 followed by cohort studies, with 24 case-control studies being least</p>

74 (Pages 290 to 293)

Kevin Holcomb, M.D.

Page 294	Page 296
<p>1 reliable."</p> <p>2 So Dr. Rothman is indicating</p> <p>3 that there is a misconception that there</p> <p>4 is a hierarchy which ranks cohort studies</p> <p>5 above case-control studies.</p> <p>6 A. He's admitting --</p> <p>7 Q. Do you see that?</p> <p>8 A. Yes. He's admitting that</p> <p>9 this is the hierarchy.</p> <p>10 Q. No. He's admitting that it</p> <p>11 is a misconception to say that cohort</p> <p>12 studies are above case-control studies.</p> <p>13 A. He's admitting that this is</p> <p>14 a common thought, right? He's saying</p> <p>15 there's a hierarchy. The misconceptions</p> <p>16 are, there's a hierarchy. So he's saying</p> <p>17 there is this thought out there that</p> <p>18 there's a hierarchy, because it's clear</p> <p>19 that there is and it's a commonly taught</p> <p>20 thing.</p> <p>21 So this one doctor is</p> <p>22 saying, similar to the doctors you</p> <p>23 brought up earlier, let's throw away</p> <p>24 convention. And I would have to read the</p>	<p>1 Q. Is that what he's saying?</p> <p>2 MS. CURRY: Object to the</p> <p>3 form.</p> <p>4 THE WITNESS: Yes, yes.</p> <p>5 BY MS. GARBER:</p> <p>6 Q. Okay. Thank you. That's</p> <p>7 the only question that I had.</p> <p>8 He's also saying, number</p> <p>9 three, "If a term that denotes the</p> <p>10 product of two factors is a regression</p> <p>11 model" -- "is a regression model is not</p> <p>12 statistically significant, then there is</p> <p>13 no biologic interaction between those</p> <p>14 factors."</p> <p>15 So again, he is attempting</p> <p>16 to debunk this notion of holding at</p> <p>17 disparate statistically significant from</p> <p>18 nonstatistically significant data,</p> <p>19 correct?</p> <p>20 MS. CURRY: Object to the</p> <p>21 form.</p> <p>22 BY MS. GARBER:</p> <p>23 Q. That's a misconception?</p> <p>24 THE WITNESS: I'm just</p>
Page 295	Page 297
<p>1 whole paper to understand why. But I</p> <p>2 take this as -- the first statement to</p> <p>3 say that there is -- he doesn't say well</p> <p>4 recognized.</p> <p>5 But I believe he took the</p> <p>6 time to write this paper to try to debunk</p> <p>7 some of these things, because they are</p> <p>8 out there and well accepted.</p> <p>9 Q. Right. They're out there,</p> <p>10 and he is concerned about that, that</p> <p>11 clinicians like yourself are putting</p> <p>12 cohort above case-control. And he's</p> <p>13 trying to debunk that because he doesn't</p> <p>14 agree with that; is that fair?</p> <p>15 MS. CURRY: Object to the</p> <p>16 form.</p> <p>17 MR. MIZGALA: Object to the</p> <p>18 form.</p> <p>19 THE WITNESS: Can I tell you</p> <p>20 that there's --</p> <p>21 BY MS. GARBER:</p> <p>22 Q. Doctor --</p> <p>23 A. -- not as much difference in</p> <p>24 what --</p>	<p>1 curious. Are you here -- are you</p> <p>2 more interested in me agreeing</p> <p>3 that you're reading this correctly</p> <p>4 or my response to it? Because I'd</p> <p>5 love to jump in and tell you about</p> <p>6 what I think about these</p> <p>7 statements. But I feel like I'm</p> <p>8 not being given an opportunity.</p> <p>9 And I -- you know, I could have</p> <p>10 come down and read all the papers</p> <p>11 that you want to read and read</p> <p>12 them out loud for you.</p> <p>13 But I'm assuming that you</p> <p>14 would like to know if I agree with</p> <p>15 it, why not if I disagree.</p> <p>16 But I feel like you keep on</p> <p>17 asking me, is that -- did I read</p> <p>18 that correctly, and I said yes,</p> <p>19 you read very well. And you say</p> <p>20 do you agree with it? And I say</p> <p>21 no.</p> <p>22 And then I go to try to</p> <p>23 explain, and you move on. And I'm</p> <p>24 trying to understand what's the</p>

75 (Pages 294 to 297)

Kevin Holcomb, M.D.

<p style="text-align: right;">Page 298</p> <p>1 purpose of that?</p> <p>2 BY MS. GARBER:</p> <p>3 Q. Are you done?</p> <p>4 A. Yes, I am.</p> <p>5 Q. Okay. You know that I am</p> <p>6 here to ask you questions, and you're</p> <p>7 here to answer questions. You also know</p> <p>8 that this is in the context of a</p> <p>9 cross-examination and your counsel has</p> <p>10 the opportunity to ask you questions too.</p> <p>11 You understand that, right?</p> <p>12 A. I understand.</p> <p>13 Q. Thanks.</p> <p>14 All right. So Dr. Rothman</p> <p>15 in his peer-reviewed and published paper</p> <p>16 indicates that there is a misconception</p> <p>17 about the hierarchy, which places cohorts</p> <p>18 above case-control. And this is a</p> <p>19 misconception about statistical</p> <p>20 significance and calling nonstatistically</p> <p>21 results different from statistical</p> <p>22 significant results.</p> <p>23 Can we agree with that?</p> <p>24 MS. CURRY: Object to the</p>	<p style="text-align: right;">Page 300</p> <p>1 that's what he's doing. I don't know the</p> <p>2 author.</p> <p>3 But to suggest that</p> <p>4 something's published and ergo it's</p> <p>5 worthwhile, that's a big misconception.</p> <p>6 Q. All right. And otherwise</p> <p>7 you agree with what I just said, if we --</p> <p>8 if we amend my question to say it is a</p> <p>9 published article --</p> <p>10 A. Can you repeat it because I</p> <p>11 got so stuck on your mentioning that it</p> <p>12 was peer-reviewed that I didn't --</p> <p>13 Q. I'll just move on.</p> <p>14 A. -- I stopped listening.</p> <p>15 Q. Did you attempt to look at</p> <p>16 what your institution said about study</p> <p>17 hierarchies?</p> <p>18 MS. CURRY: Object to the</p> <p>19 form.</p> <p>20 THE WITNESS: My</p> <p>21 institution? Which institution?</p> <p>22 BY MS. GARBER:</p> <p>23 Q. Where do you work? Where do</p> <p>24 you work?</p>
<p style="text-align: right;">Page 299</p> <p>1 form.</p> <p>2 THE WITNESS: No.</p> <p>3 BY MS. GARBER:</p> <p>4 Q. You don't agree with that?</p> <p>5 A. Because you started off the</p> <p>6 statement by saying this is</p> <p>7 peer-reviewed. This is a review article.</p> <p>8 I don't know if it's peer-reviewed.</p> <p>9 Q. It's a published article?</p> <p>10 A. It's not peer-reviewed</p> <p>11 necessarily.</p> <p>12 Q. But it's a published?</p> <p>13 A. You said peer-reviewed.</p> <p>14 Q. I know.</p> <p>15 A. I'm saying, do you know that</p> <p>16 it was peer reviewed?</p> <p>17 Q. Now I'm saying, it's a</p> <p>18 published article, right?</p> <p>19 A. Simple -- yeah, you can --</p> <p>20 it's an open access journal that you</p> <p>21 can -- I mean, just because something is</p> <p>22 published, you're making it seem like --</p> <p>23 there's something called vanity</p> <p>24 publishing. And I'm not suggesting</p>	<p style="text-align: right;">Page 301</p> <p>1 A. I work in two -- I'm</p> <p>2 actually an employee of Weill Cornell</p> <p>3 Medical Center. But I --</p> <p>4 Q. Okay. And that's your</p> <p>5 institution, right?</p> <p>6 A. As is New York Presbyterian</p> <p>7 Hospital, which is separate, so which</p> <p>8 institution --</p> <p>9 Q. You have privileges at both?</p> <p>10 A. I don't have privileges in</p> <p>11 the medical school because that's not our</p> <p>12 medical school's work. So, no, I don't</p> <p>13 have privileges --</p> <p>14 Q. You don't have privileges</p> <p>15 in -- in the hospital associated --</p> <p>16 A. The hospital is -- is owned</p> <p>17 by New York Presbyterian Hospital.</p> <p>18 Q. Okay.</p> <p>19 A. So I have no privileges at</p> <p>20 Weill Cornell.</p> <p>21 Q. Got it. I didn't understand</p> <p>22 the -- the nature of that.</p> <p>23 So did you look at Weill</p> <p>24 Cornell's study hierarchy?</p>

Kevin Holcomb, M.D.

Page 302	Page 304
<p>1 MS. CURRY: Object to the</p> <p>2 form.</p> <p>3 THE WITNESS: I don't know</p> <p>4 if -- well, no, I don't know that</p> <p>5 Weill Cornell has a study</p> <p>6 hierarchy.</p> <p>7 BY MS. GARBER:</p> <p>8 Q. Okay.</p> <p>9 (Document marked for</p> <p>10 identification as Exhibit</p> <p>11 Holcomb-17.)</p> <p>12 BY MS. GARBER:</p> <p>13 Q. Let's mark as Exhibit 17 a</p> <p>14 document.</p> <p>15 And, Doctor, this is a</p> <p>16 printout of a website from Weill Cornell.</p> <p>17 And it is titled "Evidence-based</p> <p>18 Medicine, or EBM, Defined."</p> <p>19 Did I read that correctly?</p> <p>20 A. You did.</p> <p>21 Q. Under the definition it</p> <p>22 reads, "Evidence-based medicine requires</p> <p>23 the integration of the best research</p> <p>24 evidence with our clinical expertise, and</p>	<p>1 from studies, and then brought into</p> <p>2 clinical practice.</p> <p>3 Q. Okay. And under that</p> <p>4 heading in the hierarchy at the top lists</p> <p>5 Cochrane systematic reviews. Do you know</p> <p>6 what those are?</p> <p>7 A. Yes.</p> <p>8 Q. Have you ever considered</p> <p>9 them for purposes of your practice?</p> <p>10 A. Yes.</p> <p>11 Q. You ever considered them for</p> <p>12 purposes of your opinions?</p> <p>13 A. They are part of it --</p> <p>14 MS. CURRY: Object to the</p> <p>15 form.</p> <p>16 THE WITNESS: -- yes.</p> <p>17 BY MS. GARBER:</p> <p>18 Q. And next on the top of the</p> <p>19 hierarchy is what?</p> <p>20 A. I'm not sure what SR is --</p> <p>21 systematic reviews, must be, and</p> <p>22 meta-analyses.</p> <p>23 Q. Mm-hmm. So up above the</p> <p>24 cohorts and the case-control are</p>
Page 303	Page 305
<p>1 our patients' unique values and</p> <p>2 circumstances."</p> <p>3 And then there's a citation</p> <p>4 to Straus, S-T-R-A-U-S, et al.,</p> <p>5 Evidence-based Medicine 2015.</p> <p>6 Did you see this before you</p> <p>7 put in your expert report the hierarchy</p> <p>8 that you put from the --</p> <p>9 A. No.</p> <p>10 Q. -- management website?</p> <p>11 A. No.</p> <p>12 MS. CURRY: Object to the</p> <p>13 form.</p> <p>14 BY MS. GARBER:</p> <p>15 Q. Doctor, if we could look at</p> <p>16 this together.</p> <p>17 Evidence-based medicine.</p> <p>18 That is what -- that's a -- that's a</p> <p>19 medical term, right, evidence-based</p> <p>20 medicine?</p> <p>21 A. Yes.</p> <p>22 Q. And it implies what to you?</p> <p>23 A. It implies practicing on</p> <p>24 what's deemed to be accurate findings</p>	<p>1 systematic reviews and meta-analyses,</p> <p>2 right, on this evidence-based hierarchy,</p> <p>3 right?</p> <p>4 A. Yes.</p> <p>5 Q. All right. And then there's</p> <p>6 evidence guidelines and the evidence</p> <p>7 summaries. And then one, two, three,</p> <p>8 four -- fifth down, lists randomized</p> <p>9 clinical trials, case cohorts, and</p> <p>10 control studies. All in the same line,</p> <p>11 correct?</p> <p>12 A. Yes.</p> <p>13 Q. And so that's a little</p> <p>14 different than your hierarchy, right?</p> <p>15 A. Yes.</p> <p>16 MS. CURRY: Object to the</p> <p>17 form.</p> <p>18 BY MS. GARBER:</p> <p>19 Q. And this one relates to</p> <p>20 medicine, not to management and business,</p> <p>21 right?</p> <p>22 MS. CURRY: Object to the</p> <p>23 form.</p> <p>24 THE WITNESS: Yes. It</p>

Kevin Holcomb, M.D.

Page 306	Page 308
<p>1 relates to medicine. 2 BY MS. GARBER: 3 Q. And this is from the web -- 4 this is from the -- off the website of 5 where you practice medicine? 6 A. Yes. 7 Q. And where you teach? 8 A. And where I teach. And I 9 don't necessarily disagree that a 10 well-designed -- 11 Q. Doctor, I didn't ask you if 12 you disagreed or not -- 13 A. Okay. 14 Q. -- I just asked you -- 15 A. Just to read the website. 16 MS. CURRY: Let him finish 17 his response, please. 18 BY MS. GARBER: 19 Q. Are you aware that the link 20 between smoking and lung cancer was 21 initially discovered in the case-control 22 studies carried out in the 1950s, are you 23 aware of that? 24 A. Yes.</p>	<p>1 the cohort study. And then the 2 weaknesses and biologic 3 plausibility that led me to the 4 opinion that I offered in the 5 beginning. 6 BY MS. GARBER: 7 Q. Do you believe that the 8 case-control studies are less reliable 9 than the cohort studies? 10 A. I believe that all study 11 designs can have weaknesses. And a 12 poorly designed study can come in the 13 form of any type. 14 You can have a poorly 15 designed cohort study. You can have a 16 poorly designed case-control study. You 17 can have a poorly designed meta-analysis. 18 I'm sorry, I forgot your 19 question now. 20 Q. That's okay. 21 And with regard to the 22 cohort studies, Doctor, I don't see in 23 your expert report where you talk about 24 the design limitations, specifically what</p>
Page 307	Page 309
<p>1 Q. As a physician you do 2 consider meta-analyses in your practice? 3 A. Yes. 4 Q. And as to the cohort studies 5 in this case, do you rely primarily on 6 them in support of your opinions? 7 MS. CURRY: Object to the 8 form. 9 THE WITNESS: No. As I 10 stated in the beginning, it's the 11 totality of their reviews. 12 So the cohort studies which, 13 you know, I will still say as a 14 design are less prone to bias than 15 case-control studies regardless of 16 how this is, I don't think any -- 17 anybody questions that. 18 I will look at the whole 19 picture which is what I did with 20 the talc literature. So it was 21 the inconsistency in case-control 22 results. It was the low level of 23 strength of association that I 24 found plus the lack of findings in</p>	<p>1 even the authors talk about as the design 2 limitations. 3 You don't -- you don't talk 4 about those in your expert report, right? 5 A. I'd have to read through it. 6 I'm not sure. 7 Q. Okay. 8 A. I'm not sure if I address 9 that. 10 Q. I'll represent to you that I 11 couldn't find a single word about you 12 talking about the design limitations. So 13 you can check me to see if I'm wrong. 14 You do talk about some of 15 the design limitations and the problems 16 with the case-control studies, correct? 17 A. That is true. 18 Q. And you do talk about some 19 of the design limitations and problems of 20 the meta-analyses, right? 21 A. Yes. 22 Q. And so in your opinion the 23 case-control studies do not support 24 statistically an increased risk of talcum</p>

78 (Pages 306 to 309)

Kevin Holcomb, M.D.

<p style="text-align: right;">Page 310</p> <p>1 powder product exposure and risk of 2 ovarian cancer, right? 3 A. My feeling is that the 4 case-control studies are not consistent 5 in their results. That some studies show 6 an association and some studies don't. 7 And that it seems to be as consistent as 8 flipping a coin. 9 Q. Do they support the opinion 10 that there is an increased risk, yes or 11 no? 12 A. Some do, and some don't. 13 Q. Okay. What about the -- the 14 cohort studies, do they support an 15 increased risk for -- 16 A. No. 17 Q. Let me finish my sentence. 18 A. Sorry. 19 Q. Do the cohort studies 20 support an increased risk for talcum 21 powder exposure and ovarian cancer? 22 A. The initial Gertig study had 23 found that in a subset of just 24 histologically split out there was an</p>	<p style="text-align: right;">Page 312</p> <p>1 increased risk in ovarian cancer? 2 MS. CURRY: Object to the 3 form. 4 THE WITNESS: In which 5 study? 6 BY MS. GARBER: 7 Q. In the meta-analysis as a 8 body? 9 A. Again, yes. 10 Q. Okay. The only group of 11 studies that, in your opinion, don't 12 support an increased risk, you don't have 13 a single criticism of, yet the studies 14 that do, you criticize; is that fair? 15 MS. CURRY: Object to the 16 form. 17 THE WITNESS: If you -- that 18 is true. I'm criticizing all the 19 case-control studies as a design. 20 But that means I'm criticizing the 21 ones that didn't find an 22 association just as much as I'm 23 criticizing the ones that do. 24 I'm saying at the design,</p>
<p style="text-align: right;">Page 311</p> <p>1 increased risk of serous carcinoma. The 2 reason why we're saying no about cohort 3 studies is because the same group of 4 women, when followed longer in Gates, 5 that significance dropped down. 6 So I would say overall in 7 those populations, the sister study, the 8 WHI, and the Nurses' Health Study, that 9 they did not support an increased risk. 10 Q. Do the meta-analyses as a 11 whole support an increased risk of talcum 12 powder exposure and ovarian cancer? 13 A. Not surprisingly, the 14 meta-analyses all say that the 15 case-control studies do and the cohort 16 studies don't, and when you mix the 27 17 case-control studies with the three 18 cohorts and weigh them fairly equally, 19 that you will find an increased risk when 20 you mix them altogether, which is not at 21 all surprising. 22 Q. Do the odds ratios that are 23 reported for epithelial ovarian cancer 24 and genital talc exposure support an</p>	<p style="text-align: right;">Page 313</p> <p>1 there are flaws in case-control 2 studies. And so I'm not just 3 trying to pick on the positive 4 case-control studies. I'm talking 5 about case-control studies. 6 And that's -- from my look 7 at the literature, I'm saying that 8 about half of them saying there is 9 an association and half of them 10 saying that there's not, I'm 11 criticizing case-control study 12 design altogether. 13 BY MS. GARBER: 14 Q. You said generally that 15 there can be design problems with 16 cohorts, yet I don't see a single 17 reference to the design limitations of 18 the cohorts that play in this case, 19 right? 20 A. Well, one of the concerns 21 that you can have with a cohort study is 22 whether or not you follow patients long 23 enough, whether you have sufficient size. 24 And in my read, in my</p>

Kevin Holcomb, M.D.

<p style="text-align: right;">Page 314</p> <p>1 understanding of the data, I was not 2 concerned -- size I already explained, 3 that I was concerned since it was such a 4 small level of effect in the case-control 5 studies. It wasn't until I saw Berge, 6 when they put them together, that I 7 realized that you could overcome that 8 size problem. And so I was not concerned 9 that you would pick up an effect size 10 that small. 11 Q. Do you remember what my 12 question was? 13 A. Yes. You asked me did I 14 bring up criticisms. And I'm saying my 15 criticisms about cohort studies in 16 general, I was able to put to rest with 17 my reading of those cohort studies, 18 whereas things like recall bias -- and we 19 already went through Schildkraut -- I was 20 able to find examples of why I was 21 concerned, and then find examples of 22 studies where I thought they were at 23 play. 24 So, I'm just explaining to</p>	<p style="text-align: right;">Page 316</p> <p>1 true, Doctor, that none of the cohort 2 studies were specifically designed to 3 investigate the relationship of talcum 4 powder product use and the risk of 5 ovarian cancer? 6 MS. CURRY: Object to the 7 form. 8 THE WITNESS: Specifically 9 no. 10 BY MS. GARBER: 11 Q. Rather, the cohorts were 12 designed to study a large number of 13 outcomes in a wide variety of exposures, 14 true? 15 A. True. When you do a cohort 16 study, because of the time and money 17 invested, you are very rarely going to 18 design a cohort study to answer one 19 question. 20 Q. Right. And that's a 21 limitation, right? 22 MS. CURRY: Object to the 23 form. 24 THE WITNESS: I'm not</p>
<p style="text-align: right;">Page 315</p> <p>1 you, you're saying, why is there an 2 absence of criticisms on these things. I 3 didn't find any evidence of those things 4 at play in the cohort studies. 5 Q. So you didn't find as the 6 expert for Johnson & Johnson in the 7 studies that didn't find an increased 8 risk in your opinion, and you didn't 9 bother to advise the court that there are 10 design limitations in that group of 11 studies, the cohorts, yet you did tell 12 the court about the study limitations of 13 the case-control and the study 14 limitations of the meta-analyses, true? 15 MS. CURRY: Object to the 16 form. 17 BY MS. GARBER: 18 Q. I didn't ask why. I just 19 said true. 20 A. True. 21 Q. Thank you. 22 All right. Let's look at a 23 couple of things. So in looking at the 24 cohort studies and the limitations, is it</p>	<p style="text-align: right;">Page 317</p> <p>1 sure -- 2 BY MS. GARBER: 3 Q. It's okay. 4 A. -- in what way that was a 5 limitation. 6 Q. You're not sure? 7 A. No. 8 Q. Okay. With a cohort study 9 looking at a rare cancer like ovarian 10 cancer, the study has to be large enough 11 to detect the true relative risk. 12 Do you agree with that? 13 A. I agree. 14 Q. So in fact, that a cohort 15 does not find a significant relative risk 16 can be due to the small study size, 17 correct? 18 MS. CURRY: Object to the 19 form. 20 THE WITNESS: Correct. 21 BY MS. GARBER: 22 Q. The sample sizes and the 23 number of cases of most of the cohort 24 study publications were too small to be</p>

80 (Pages 314 to 317)

Kevin Holcomb, M.D.

<p style="text-align: right;">Page 318</p> <p>1 able to accurately detect a relative risk 2 around 1.2 to 1.3. 3 Do you agree with that 4 statement? 5 MS. CURRY: Object to the 6 form. 7 THE WITNESS: I'm not sure. 8 I -- I've seen the opinion 9 expressed in the Narod paper that 10 you -- you had produced earlier. 11 And I keep on referring to Berge 12 only because it was the one 13 meta-analysis where they actually 14 addressed that. 15 Narod said you need like 16 200,000 women to see this effect 17 size, and then you look at three 18 studies with 78,000, 61,000, 19 41,000. You're getting close to 20 that 200,000. They say, we have 21 99 percent power to detect the 22 effect size in a meta-analysis 23 that is held so highly to see the 24 same effect size in the</p>	<p style="text-align: right;">Page 320</p> <p>1 your study and then coming out 2 with spurious values. 3 And one of the first things 4 that is generally thought to be a 5 no-no, we don't do cross-trial 6 comparisons in general. If you 7 had a group of women taking this 8 chemotherapy over here and a group 9 of women taking chemotherapy over 10 there, we don't compare those two 11 chemotherapies and say well, this 12 study showed a response rate of 13 this. This showed this, this, 14 that. 15 So whenever you're going 16 against that rule and you're going 17 to mix these people together, you 18 want to make sure that there's not 19 heterogeneity. And the reason why 20 I keep on going back to Berge, is 21 because Penninkilampi somehow 22 looked at pretty much the same 23 studies and did not find a problem 24 with heterogeneity, whereas Berge</p>
<p style="text-align: right;">Page 319</p> <p>1 case-control studies. 2 BY MS. GARBER: 3 Q. Well, you do go to Berge all 4 the time. But you do that by ignoring 5 Penninkilampi which was a more recent 6 study, right? 7 A. But the problem -- 8 MS. CURRY: Object to the 9 form. 10 THE WITNESS: The problem -- 11 the problem with Penninkilampi is 12 that Berge says the first thing 13 out the box is I'm going to look 14 at heterogeneity and see if these 15 should be mixed. And one of the 16 problems with putting 17 meta-analyses on the top of your 18 thing is assuming it's well 19 designed. 20 And I think all these 21 studies can have design flaws. 22 But I think meta-analysis is 23 probably the most at risk for 24 making mistakes in the design of</p>	<p style="text-align: right;">Page 321</p> <p>1 says yeah, I found this 2 difference, but I'll caution you, 3 don't take it too seriously 4 because there was too much 5 heterogeneity in these two study 6 designs. 7 And I'm just questioning, 8 how is it that Berge was able to 9 find this heterogeneity issue and 10 yet other -- Taher, Penninkilampi, 11 other people who looked at largely 12 overlap the same study group, with 13 very little difference, somehow 14 didn't come up with this problem. 15 BY MS. GARBER: 16 Q. So -- 17 A. And so I keep on going back 18 to it because it's the only meta-analysis 19 that says okay, here is the group if we 20 put them altogether. Maybe we shouldn't 21 be doing it in the first place. But 22 we're going to do it. 23 We put them altogether, but 24 here is what it looks like if you leave</p>

Kevin Holcomb, M.D.

<p style="text-align: right;">Page 322</p> <p>1 them separately.</p> <p>2 Q. So, Doctor, if you would</p> <p>3 then look at the Penninkilampi</p> <p>4 meta-analysis which is later than the</p> <p>5 Berge meta-analysis, right?</p> <p>6 A. Yes.</p> <p>7 Q. And the Berge meta-analysis,</p> <p>8 and you say that those are basically the</p> <p>9 same studies that the two study groups --</p> <p>10 A. There's a lot of overlap.</p> <p>11 Q. -- studied, right?</p> <p>12 And the Penninkilampi says</p> <p>13 there's no heterogeneity. And the Berge</p> <p>14 that says there is. What is your basis</p> <p>15 to say Berge is right and Penninkilampi</p> <p>16 is wrong?</p> <p>17 A. Because if you can share --</p> <p>18 Q. You don't like the results</p> <p>19 of Penninkilampi?</p> <p>20 A. -- if you can share -- yes.</p> <p>21 If you can share Penninkilampi, because</p> <p>22 Berge the -- Berge, Berge, I don't know</p> <p>23 if I'm pronouncing it correctly, sorry.</p> <p>24 Q. However you say it.</p>	<p style="text-align: right;">Page 324</p> <p>1 remember them splitting out the case</p> <p>2 controls and the -- they -- they do say</p> <p>3 all the impact -- the positive effect was</p> <p>4 in case-control, not in cohort studies.</p> <p>5 Taher does say that.</p> <p>6 Although Taher, if you look</p> <p>7 at the tables, there's a few things that</p> <p>8 I don't understand. Like they -- they</p> <p>9 say, actually in the cohort studies that</p> <p>10 there is some increased risk of -- of</p> <p>11 ovarian cancer.</p> <p>12 And they -- they are</p> <p>13 actually including Gates in that. And</p> <p>14 they say there's possibly an increased</p> <p>15 risk in -- in Gates. And then go onto</p> <p>16 say, "but not mucinous."</p> <p>17 But in Gates there was no</p> <p>18 increased risk of any of the types. In</p> <p>19 fact, the only one that came the closest</p> <p>20 to it was mucinous.</p> <p>21 Q. We're going to get to that,</p> <p>22 and we'll go through that data, okay?</p> <p>23 A. Sure.</p> <p>24 Q. Let's look at Health Canada</p>
<p style="text-align: right;">Page 323</p> <p>1 A. The first thing they do is</p> <p>2 to talk about heterogeneity in study</p> <p>3 design. And I'd like to see in</p> <p>4 Penninkilampi to say that they considered</p> <p>5 study design heterogeneity and found</p> <p>6 none. Because I don't remember seeing</p> <p>7 that. I'd like to see the paper if you</p> <p>8 have it. But I don't remember them even</p> <p>9 addressing it.</p> <p>10 He goes into act -- other</p> <p>11 lesser important areas of heterogeneity</p> <p>12 like the percentage that looked at mode</p> <p>13 of exposure and things like that.</p> <p>14 So if one doesn't even</p> <p>15 mention it, and one mentions it and says</p> <p>16 we found heterogeneity, I don't assume</p> <p>17 that the one who didn't even mention it,</p> <p>18 looked at it, found heterogeneity and</p> <p>19 just decided not to mention it. I'm</p> <p>20 assuming they didn't think about it.</p> <p>21 Q. What did the Taher paper say</p> <p>22 about heterogeneity? Was there a</p> <p>23 significant overlap in the Taher paper?</p> <p>24 A. I don't remember -- I don't</p>	<p style="text-align: right;">Page 325</p> <p>1 as to the topic of case-control -- or</p> <p>2 cohort studies.</p> <p>3 A. Yes.</p> <p>4 Q. Page 20.</p> <p>5 All right. On Page 20 in</p> <p>6 this paragraph here. Do you see where I</p> <p>7 am in the -- in the Taher paper?</p> <p>8 A. Yes, I see it.</p> <p>9 Q. Or, sorry, Health Canada.</p> <p>10 It indicates -- I'll -- I'll</p> <p>11 start with the first given.</p> <p>12 "Given the long latency</p> <p>13 period of ovarian cancer, the follow-up</p> <p>14 periods may not have been sufficient to</p> <p>15 capture all cases for the individual</p> <p>16 cohort studies.</p> <p>17 "Also, given the rarity of</p> <p>18 ovarian cancer, many of the available</p> <p>19 human studies may not be sufficiently</p> <p>20 powered to detect a low odds ratio."</p> <p>21 Do you agree with both of</p> <p>22 those statements?</p> <p>23 A. No.</p> <p>24 Q. Which ones do you --</p>

Kevin Holcomb, M.D.

Page 326	Page 328
<p>1 A. I'll start off.</p> <p>2 Q. Do you agree with either</p> <p>3 one?</p> <p>4 A. I -- I'll start off. The</p> <p>5 long latency for ovarian cancer suggests</p> <p>6 we know the latency for ovarian cancer.</p> <p>7 To determine the latency for a cancer you</p> <p>8 have to know the time from exposure to a</p> <p>9 carcinogen to the time it develops.</p> <p>10 So most people who make</p> <p>11 statements about ovarian cancer latency</p> <p>12 will look at things like women who</p> <p>13 developed ovarian cancer after the</p> <p>14 dropping of the atomic bomb at Hiroshima.</p> <p>15 They'll look at the chance of developing</p> <p>16 ovarian cancer after heavy occupational</p> <p>17 exposure to asbestos.</p> <p>18 You have to know the</p> <p>19 carcinogen first before you can determine</p> <p>20 the latency. So they are assuming, well,</p> <p>21 if there is long latency in these</p> <p>22 situations it should be the same. But</p> <p>23 instead it's taken as a given.</p> <p>24 Given the long latency of</p>	<p>1 MS. CURRY: I'm sorry.</p> <p>2 You -- you've asked three</p> <p>3 questions already that he's trying</p> <p>4 to respond to. So we'll still on</p> <p>5 question Number 1 as to why he</p> <p>6 disagrees with these two</p> <p>7 statements.</p> <p>8 BY MS. GARBER:</p> <p>9 Q. I just -- I just now asked</p> <p>10 you if you have an opinion as to the</p> <p>11 latency period.</p> <p>12 A. I was -- yeah, I'm -- I'm</p> <p>13 trying to keep my train of thought</p> <p>14 steady. And I'm sure you want to keep</p> <p>15 yours steady as well.</p> <p>16 So I'm going to finish</p> <p>17 answering the first thing you asked and</p> <p>18 then we'll get to that.</p> <p>19 Q. Okay.</p> <p>20 A. So sample sizes were not</p> <p>21 large enough to detect the 20 to</p> <p>22 30 percent increased risk. And as you</p> <p>23 said, I keep going back to Berge, because</p> <p>24 they say yes, there was enough.</p>
Page 327	Page 329
<p>1 ovarian cancer. Latency to what?</p> <p>2 Latency from what incident? There --</p> <p>3 latency from --</p> <p>4 Q. Do you have an opinion of</p> <p>5 the years?</p> <p>6 A. Excuse me?</p> <p>7 Q. Do you have an opinion of</p> <p>8 the years of latency --</p> <p>9 A. I -- I'm just letting --</p> <p>10 Q. -- of ovarian cancer?</p> <p>11 A. I'm saying that you --</p> <p>12 MS. CURRY: Object to the</p> <p>13 form. And were you done with your</p> <p>14 prior answer?</p> <p>15 THE WITNESS: No. Because I</p> <p>16 didn't go through the other part.</p> <p>17 And then -- but going back</p> <p>18 to the other one where they say --</p> <p>19 BY MS. GARBER:</p> <p>20 Q. Sorry, Doctor, can I</p> <p>21 interrupt you?</p> <p>22 Do you have an opinion --</p> <p>23 A. I'd like to finish my first</p> <p>24 answer.</p>	<p>1 If you add those three</p> <p>2 cohort studies, you had 99 percent chance</p> <p>3 of picking up what was in the</p> <p>4 case-control studies, but yet Taher</p> <p>5 says -- or, sorry, Health Canada says</p> <p>6 that there may not have been enough. But</p> <p>7 they -- and then they -- they quote Narod</p> <p>8 as opposed to quoting -- there's no</p> <p>9 mention of Berge saying that there was</p> <p>10 enough. There's just Narod's op Ed</p> <p>11 opinion in 2016 which was not based on a</p> <p>12 single study. So I didn't -- so I didn't</p> <p>13 agree with either one.</p> <p>14 Q. So the Narod paper is</p> <p>15 talking in the abstract about the design</p> <p>16 of cohort studies, and that you need a</p> <p>17 sufficient number to detect a low odds</p> <p>18 ratio.</p> <p>19 The Berge study is talking</p> <p>20 about their study, his study, right?</p> <p>21 A. Berge was a meta-analysis.</p> <p>22 Q. Yeah. And -- and they're</p> <p>23 talking about, for purposes of power,</p> <p>24 that study. Narod is talking about in</p>

Kevin Holcomb, M.D.

Page 330	Page 332
<p>1 general when you look at cohort studies, 2 they have to have sufficient number of -- 3 of study participants or you are not 4 going to detect a small risk. 5 A. In the same way that I 6 wouldn't look at -- 7 MS. CURRY: Object to the 8 form. 9 THE WITNESS: -- 10 occupational exposure to asbestos 11 to answer the question of what 12 talc does when dusted on the 13 perineum, I wouldn't stick on a 14 hypothetical statement by Narod 15 when you actually have data from 16 women in the clinical scenario 17 that you're questioning, do you or 18 do you not have the power to 19 detect the level of -- the low 20 level of effect. 21 They are admitting it's a 22 low level. They are saying that 23 maybe it wasn't enough. But I'm 24 saying there's a study out there</p>	<p>1 assumptions get made over and over 2 and over of what the latency 3 period is. And you asked me then, 4 do I have an opinion on what the 5 latency period is. 6 And I can say that if you 7 had heavy occupational exposure 8 to -- I'll let you finish. 9 BY MS. GARBER: 10 Q. No. Carry on. Carry on. 11 A. No, I'll let you finish. 12 Q. I can do two things at once. 13 I can multitask. I'm listening. I'm 14 listening. 15 A. All right. So if you -- if 16 you're asking me what is the latency 17 period for someone making gas masks in a 18 factory, I would say it's probably 19 somewhere around 20 years, maybe 20 30 years. Hiroshima, you know, maybe 10 21 to 20 years. That's the question. 22 Q. So you have testified in a 23 prior case that ovarian cancer has a long 24 latency; is that true?</p>
Page 331	Page 333
<p>1 that says it was enough and gives 2 the explanation with the numbers. 3 It's not -- it's not cited 4 here. 5 BY MS. GARBER: 6 Q. Doctor, you recognize that 7 Health Canada is recognizing that the 8 latency for development of ovarian cancer 9 is an important issue in the cohort 10 designs, right? 11 MS. CURRY: Object to the 12 form. 13 THE WITNESS: I'm -- I'm not 14 requesting that. I'm questioning 15 what is the latency from. If you 16 assume that talc causes ovarian 17 cancer, what is the latency for 18 talc causing ovarian cancer? 19 No one knows. So any 20 extrapolation is an extrapolation 21 from another situation like an 22 atomic bomb, like in a heavy 23 occupational exposure. So there 24 is an assumption, and these</p>	<p>1 MS. CURRY: Object to the 2 form. 3 THE WITNESS: In those 4 situations. 5 BY MS. GARBER: 6 Q. Yeah. All right. 7 And you have testified that 8 it can be as long as 20 to 40 years, 9 correct? 10 A. It's possible, yes. Based 11 on the extrapolations I just mentioned. 12 Q. And you're aware of the 13 Purdie study from 2003 that indicated the 14 latency as likely 30 to 40 years, 15 correct? 16 A. Can you show me Purdie study 17 and I can see what they're relying on -- 18 Q. Sure. 19 A. -- and see what citation 20 they use, or if it's cited at all. 21 (Document marked for 22 identification as Exhibit 23 Holcomb-18.) 24 BY MS. GARBER:</p>

Kevin Holcomb, M.D.

Page 334	Page 336
<p>1 Q. Let's mark as Exhibit 18. 2 The Purdie 2003 study. 3 Doctor, if you turn to Page 4 231. Following Footnote 23, it reads, 5 "With regard to the latency" -- 6 A. I'm sorry. 231. 7 Following -- you said -- 8 Q. Here. Look up here, Doctor. 9 A. Hold on one second. 10 Q. The authors state, "It is 11 likely that ovarian cancer has a 12 reasonable" -- 13 A. I'm sorry. Can you -- I 14 really want to read along with you. I 15 just don't see where you are. You said 16 231 is the page we're on? 17 Q. Yes. 18 A. Okay. Left? Right? 19 Q. Left-hand column. 20 A. Okay. Top of the page, 21 middle of the page, bottom? 22 Q. Right here. "It is likely 23 that ovarian cancer has a reasonably long 24 latency period between initiation and</p>	<p>1 bit it says -- couple lines, it says, 2 "Thus, the latency period of more 3 advanced malignant epithelial ovarian 4 cancer could be estimated to be 5 approximately 30 to 40 years." 6 A. "This time frame is 7 consistent with data from the Hiroshima 8 cohort." 9 Yes. They're doing what I 10 said. They're extrapolating from an 11 atomic bomb victim to figure out what the 12 latency would be for somebody putting 13 talcum powder in their underwear. 14 Q. And, Doctor, do you have any 15 reason or basis -- strike that. 16 Do you have any basis to 17 claim that the latency period would be 18 any different for talcum powder exposure 19 and development of ovarian cancer? 20 A. In the totality of my review 21 of the literature, I don't see sufficient 22 evidence to consider that talcum powder 23 even causes ovarian cancer. So I don't 24 have a carcinogen to start off with to</p>
Page 335	Page 337
<p>1 manifestation of established disease, and 2 this is exacerbated by unusually late 3 clinical detection of the disease." 4 A. And that -- 5 Q. And you agree -- you 6 disagree with that? 7 MS. CURRY: Object to the 8 form. I think you said unusually. 9 The word is usually. 10 BY MS. GARBER: 11 Q. Do you disagree with that 12 statement? 13 A. What I -- I was curious to 14 see what the citation was. I would say 15 that in other situations with a known 16 carcinogen, like the radiation from an 17 atomic bomb or heavy occupational 18 exposure, in those situations there is a 19 long latency. 20 Q. And so, Doctor -- 21 A. Here there's no citations. 22 So I'm not sure what the statement is 23 based on. 24 Q. So, Doctor, if you go down a</p>	<p>1 start estimating latency. 2 What they're saying is, if 3 you extrapolate from the few situations 4 that we know that cause ovarian cancer, 5 they have a long latency. So the 6 assumption is, well, this must have a 7 long latency period too. 8 They've given no citation 9 why that it is likely. It's just, well, 10 it happened here; it must be the same 11 here. 12 Q. So let's talk about this. 13 You're a study designer. And you really 14 want to find out if talcum powder 15 exposure causes ovarian cancer. And you 16 know that there's all this data out here 17 that ovarian cancer has a long latency. 18 A. It's all this data out here? 19 Q. Yeah. I'm giving you a 20 hypothetical. There's data from 21 radiation and other exposures. Okay? 22 A. Okay. 23 Q. And the latency period is 24 about 20 to 40 years. Are you going to</p>

85 (Pages 334 to 337)

Kevin Holcomb, M.D.

<p style="text-align: right;">Page 338</p> <p>1 design a study that is going to follow 2 women 10 or six or 15 years when you know 3 that potentially it could be 20, 4 40 years? You're not going to detect all 5 the risk, are you? 6 MS. CURRY: Object to the 7 form. 8 THE WITNESS: I think 9 there's a misconception between 10 how long you follow a patient and 11 latency. 12 Latency doesn't start when 13 you designed a study and she 14 signed the consent form. Latency 15 started from exposure to 16 development of a cancer. 17 So if somebody, let's say, 18 on the woman's health initiative, 19 is 55 at the time that she goes 20 on, and you're trying to convince 21 me earlier that this is this 22 habitual thing that she does, that 23 she doesn't even think about it. 24 Cramer 2016 says she likely</p>	<p style="text-align: right;">Page 340</p> <p>1 ovarian cancer is the biologic 2 plausibility and where it falls 3 apart on dose-response. 4 So I'm saying, just because 5 you followed somebody from 6 12 years, doesn't mean that they 7 started using talc the day before 8 she signed consent. 9 And so no, if you're talking 10 about a behavior that likely 11 starts in the 20s, and you're 12 trying to design a study that's 13 enrolling women who started at 50, 14 yeah, 12 years should be enough. 15 BY MS. GARBER: 16 Q. Doctor, in the studies 17 themselves, do they indicate when the 18 women started using the talc, the age at 19 which they started using the talc? 20 MS. CURRY: Object to the 21 form. 22 THE WITNESS: Again, no. I 23 am referring to what Dr. Cramer 24 believes.</p>
<p style="text-align: right;">Page 339</p> <p>1 started in her 20s. She may be 2 decades in by the time that you're 3 following her. 4 So if somebody has been 5 using talc for 20 years and then 6 you follow them for another 12, or 7 in the case of Gates, they were 8 followed for 24 years, and they 9 showed even women who had greater 10 than 20 years' exposure didn't 11 have an increased risk. 12 The other problem with this 13 concept that you're having, like 14 you're missing the latency, you 15 would expect that even in the 16 studies that are showing an 17 effect, that you should be able to 18 show a dose-response curve with 19 duration of use. And it's an 20 inconsistent thing. And all the 21 data, it's inconsistent. 22 There's -- one of the 23 struggles of saying that this 24 is -- that talc is a cause of</p>	<p style="text-align: right;">Page 341</p> <p>1 BY MS. GARBER: 2 Q. You're making assumptions 3 based on one given study -- 4 MS. CURRY: Objection. 5 BY MS. GARBER: 6 Q. -- as to when the women were 7 exposed to talc. Isn't that true? 8 MS. CURRY: Object to the 9 form. 10 THE WITNESS: Honest -- no. 11 Honestly it's -- it's also 12 personal experience with just 13 people in my family who have used 14 talc. It's been -- it hasn't been 15 my experience. I -- I don't know 16 anybody -- 17 BY MS. GARBER: 18 Q. That's not scientific, 19 Doctor, is it? 20 A. It's not. No. But you 21 asked me what it's based on. I'm saying 22 I don't know anybody who starts using 23 talc and never did it before and they 24 started at 50.</p>

86 (Pages 338 to 341)

Kevin Holcomb, M.D.

Page 342	Page 344
<p>1 Q. Okay. And if you were going 2 to take my history if I were one of your 3 patients and you wanted to find out about 4 my risk for developing lung cancer, you 5 wanted to find out about my smoking 6 history, ask me what questions you 7 would -- and tell me what questions you 8 would ask me. 9 A. I would ask -- 10 MS. CURRY: Object to the 11 form. 12 BY MS. GARBER: 13 Q. About my exposure? 14 A. I would ask when you started 15 smoking cigarettes. How many cigarettes 16 a day do you smoke. 17 Q. What else? 18 A. Have you been exposed to 19 asbestos. I know that's a co-carcinogen. 20 Things like that. 21 Q. So when I started. 22 A. Mm-hmm. 23 Q. And how -- 24 A. Do you still smoke today?</p>	<p>1 Q. Doctor, I'm going to mark 2 the Gertig 2000 study -- 3 (Document marked for 4 identification as Exhibit 5 Holcomb-19.) 6 BY MS. GARBER: 7 Q. -- as -- I'm sorry -- as 8 Exhibit 19. 9 Doctor, a study limitation 10 of the Nurses' Health Study is that the 11 authors only captured talcum powder 12 exposure one time in 1982 via 13 questionnaire, right? 14 A. It's true. 15 Q. Another limitation is the 16 study's exposure metric only captured 17 frequency of use, and not cumulative use, 18 correct? 19 MS. CURRY: Object to the 20 form. 21 THE WITNESS: Yes. 22 BY MS. GARBER: 23 Q. And Table 2 shows that the 24 talc use in the perineum is never less</p>
Page 343	Page 345
<p>1 Q. -- how frequently I smoke? 2 A. Mm-hmm. 3 Q. And so that's a two-sided 4 metric, right, frequency and duration. 5 A. Right. 6 Q. Right? And that's important 7 to determine the true risk? 8 MS. CURRY: Object to the 9 form. 10 BY MS. GARBER: 11 Q. Right? 12 MS. CURRY: Object to the 13 form. 14 THE WITNESS: That's true. 15 MS. GARBER: Okay. Let's 16 take a break. 17 THE VIDEOGRAPHER: Okay. 18 Stand by, please. The time is 19 3:28 p.m. Off the record. 20 (Short break.) 21 THE VIDEOGRAPHER: Okay. We 22 are back on the record. The time 23 is 3:55 p.m. 24 BY MS. GARBER:</p>	<p>1 than one week, one to -- one to six -- 2 sorry. 3 Less than one time per week, 4 one to six times per week, and daily, 5 correct, is that your understanding? 6 A. Yes. 7 Q. And an adequate 8 dose-response cannot be determined by 9 just measuring frequency without the 10 length of use, correct? 11 MS. CURRY: Object to the 12 form. 13 BY MS. GARBER: 14 Q. Do you agree with that? 15 A. No, I don't agree. 16 Q. Okay. Because the 17 assessment was only made in 1982, many of 18 the women may have stopped using talcum 19 powder products over the study period. 20 Do you agree with that? 21 A. Not likely. 22 Q. Do you agree that there were 23 only 78,630 women who formed the cohort 24 analysis?</p>

87 (Pages 342 to 345)

Kevin Holcomb, M.D.

<p style="text-align: right;">Page 346</p> <p>1 A. Yes.</p> <p>2 Q. That's a far cry from the</p> <p>3 requisite 200 of the Narod study,</p> <p>4 correct?</p> <p>5 MS. CURRY: Object to the</p> <p>6 form.</p> <p>7 THE WITNESS: I've already</p> <p>8 addressed that in the past.</p> <p>9 BY MS. GARBER:</p> <p>10 Q. All right. You didn't --</p> <p>11 and didn't you testify in the Ingham case</p> <p>12 that we don't know if there was a proper</p> <p>13 control group because we don't know if</p> <p>14 the control group was exposed to talcum</p> <p>15 powder products via diapering?</p> <p>16 MS. CURRY: Object to the</p> <p>17 form.</p> <p>18 THE WITNESS: You'd have to</p> <p>19 show me my --</p> <p>20 BY MS. GARBER:</p> <p>21 Q. You don't recall testifying</p> <p>22 about that?</p> <p>23 A. We talked -- I'd be happy to</p> <p>24 read through it again. I don't have an</p>	<p style="text-align: right;">Page 348</p> <p>1 under the multivariant relative risk,</p> <p>2 right?</p> <p>3 A. Yes. Earlier you had said</p> <p>4 reference. So yes. It's 1.09.</p> <p>5 Q. That's an elevated risk,</p> <p>6 right?</p> <p>7 THE VIDEOGRAPHER: Can you</p> <p>8 give me one second. Sorry. Just</p> <p>9 lost power in my camera for some</p> <p>10 reason.</p> <p>11 Stand by. The time is</p> <p>12 3:59 p m. Off the record.</p> <p>13 (Brief pause.)</p> <p>14 THE VIDEOGRAPHER: Okay. We</p> <p>15 are back on the record. The time</p> <p>16 is 4:00 p m.</p> <p>17 BY MS. GARBER:</p> <p>18 Q. And, Doctor, before that</p> <p>19 break, I was just asking you about ever</p> <p>20 use of perineal talc -- ever perineal</p> <p>21 talc use. And I asked you, is a</p> <p>22 multivariant relative risk 1.09 with a</p> <p>23 confidence interval of 0.86 to 1.37. And</p> <p>24 you agreed that that's what it is,</p>
<p style="text-align: right;">Page 347</p> <p>1 independent memory of that.</p> <p>2 Q. All right. The Gertig paper</p> <p>3 provided a result for ever use of talcum</p> <p>4 powder products on the perineum for</p> <p>5 ovarian cancer at Table 2. Do you recall</p> <p>6 that?</p> <p>7 A. Yes.</p> <p>8 Q. And I'll just show you</p> <p>9 Table 2 here. Table 2, ever perineal</p> <p>10 talc use, yes, no.</p> <p>11 Correct?</p> <p>12 A. Correct.</p> <p>13 Q. All right. And the point</p> <p>14 estimate for ever use of talc, talc</p> <p>15 powder products and EOC was 1.9 with a</p> <p>16 confidence interval of 0.86 to 1.37; is</p> <p>17 that correct?</p> <p>18 A. No. The reference is by</p> <p>19 Definition 1.</p> <p>20 Q. The ever use.</p> <p>21 A. I'm sorry.</p> <p>22 Q. The ever use --</p> <p>23 A. Yes.</p> <p>24 Q. -- point estimate was 0.09</p>	<p style="text-align: right;">Page 349</p> <p>1 correct?</p> <p>2 A. Yes.</p> <p>3 Q. That's an elevated risk,</p> <p>4 correct?</p> <p>5 MS. CURRY: Object to the</p> <p>6 form.</p> <p>7 THE WITNESS: No. That's --</p> <p>8 you can't say for sure whether</p> <p>9 that's an elevated risk. Because</p> <p>10 the true risk estimate is</p> <p>11 somewhere between having a 14 --</p> <p>12 yeah, 14 percent reduction in risk</p> <p>13 to a 37 percent increase in risk.</p> <p>14 And the true risk is somewhere in</p> <p>15 there. Where exactly the true</p> <p>16 risk estimate I'm not sure.</p> <p>17 BY MS. GARBER:</p> <p>18 Q. The point estimate, the</p> <p>19 point estimate is elevated at 1.09, true?</p> <p>20 MS. CURRY: Object to the</p> <p>21 form.</p> <p>22 THE WITNESS: The point</p> <p>23 estimate is elevated, yes.</p> <p>24 BY MS. GARBER:</p>

88 (Pages 346 to 349)

Kevin Holcomb, M.D.

<p style="text-align: right;">Page 350</p> <p>1 Q. And the follow-up study 2 period was just 14 years, correct, here 3 at Table 2, it sets forth a follow-up 4 period. 5 If you look here at the 6 table, you see the study period? 7 A. Okay -- 8 Q. It's 14 years, right? 9 A. One second. I'm just doing 10 the math. I went to public school. 11 Q. Okay. I went to a private 12 school. But I'm not good at math either. 13 A. Yes, 14 years. 14 Q. Okay. And with regard to 15 that follow-up period at Page 251, 16 Doctor, the authors note the limitation 17 in that they state, "In that regard, in 18 the peer-reviewed paper" -- 19 MS. CURRY: I'm sorry, where 20 are you -- 21 THE WITNESS: I'm sorry, I 22 don't know where you're reading. 23 BY MS. GARBER: 24 Q. I'm reading at the top of</p>	<p style="text-align: right;">Page 352</p> <p>1 limitations that I just went through with 2 you are cited or addressed in your expert 3 report; is that true? 4 A. That's true. I did not 5 consider that a -- while a potential 6 study limitation, I sort of -- I looked 7 at the literature in totality, and other 8 papers suggested that while they could 9 not account for it, it's very likely that 10 this was a practice that began early in 11 the women's lives. 12 And so for completeness' 13 sake, they are mentioning this as a 14 limitation. But the follow-up period, as 15 I mentioned earlier, of 14 years would be 16 too short to pick up a latency of 17 15 years if the woman just started using 18 talc the day she signed the consent. But 19 if she had used talc for just three years 20 before signing the consent, it would not 21 have been a weakness. 22 So I respect them mentioning 23 this for completeness' sake. But the 24 likelihood of them having not enough time</p>
<p style="text-align: right;">Page 351</p> <p>1 251, right-hand column. The authors 2 state, "Our relatively short follow-up 3 period may be inadequate to detect an 4 association if the latency for 5 development of ovarian cancer is more 6 than 15 years." 7 Did I read that correctly? 8 A. You read that correctly. 9 Q. So the authors are noting 10 that study limitation, correct? 11 A. Yes, they did. 12 Q. Also, at 251, the authors in 13 the middle column note that there are 14 several important study limitations, 15 correct? 16 A. That's what it says, yes. 17 Q. The authors also note that 18 they cannot determine the age at which 19 women began using talc or the duration of 20 their use. That's what they say under 21 the heading of "Several Important 22 Limitations in Our Study," right? 23 A. Yes. 24 Q. Okay. None of those study</p>	<p style="text-align: right;">Page 353</p> <p>1 for latency -- because latency again is 2 not follow-up time, it's exposure to 3 diagnosis -- I think it's unlikely that 4 they would not have the latency if you 5 extrapolated from an atomic bomb victim. 6 Q. Did I ask you why those 7 aren't -- those study limitations aren't 8 contained within your expert report? 9 A. No. You asked me if it was 10 mentioned. And I was just explaining why 11 it wasn't. 12 Q. Try to just answer my 13 questions, if you can, Doctor. I really 14 appreciate it. 15 The relative risk for ever 16 use of talcum powder products in serous 17 invasive ovarian cancer was elevated at 18 1.4 with a confidence interval of 1.02 to 19 1.91, correct? 20 A. It depends on what type of 21 use you're talking about. Because 22 strangely enough, in this study, for some 23 reason, if you use talcum powder on your 24 perineum, but you also used it on</p>

Kevin Holcomb, M.D.

Page 354	Page 356
<p>1 sanitary napkins, an increased exposure, 2 the point estimates are actually 3 protective, there's .89, of course 4 crossing one, and .90. So -- 5 Q. Doctor, what was my 6 question? 7 A. You said ever use of what 8 type. 9 MS. CURRY: Did you complete 10 your thought? 11 BY MS. GARBER: 12 Q. So, Doctor, you'll get a 13 chance to answer questions that counsel 14 for Johnson & Johnson may want to ask 15 you. 16 My question was, is the odds 17 ratio for serous ovarian cancer 1.4 with 18 a confidence interval of 1.02 to 1.91? 19 Is that what's reported in the study? 20 A. I'm sorry. One second, 21 ma'am. For multivariate, it's 1.4, yes. 22 Q. Okay. And serous ovarian 23 cancer, as you testified several hours 24 ago, is a type of ovarian cancer,</p>	<p>1 So if Gates has 24 years of 2 follow-up, I would look at Gates 3 as the answer to this. 4 So that's exactly what 5 happened in this situation. These 6 same group of women followed years 7 later, closer to covering the 8 latency that you were concerned 9 about, this risk went away. 10 And so I don't think I would 11 report twice on the same cohort of 12 patients. 13 MS. GARBER: Objection. 14 Motion to strike as nonresponsive. 15 BY MS. GARBER: 16 Q. Doctor, you didn't cite in 17 the four corners of your expert report 18 that the Gertig study showed an increased 19 risk in serous ovarian cancer, did you? 20 MS. CURRY: Object to the 21 form. 22 THE WITNESS: I just 23 explained why I made the general 24 statement --</p>
Page 355	Page 357
<p>1 correct? 2 A. The most predominate type, 3 yes. 4 Q. Okay. And so when you say 5 in your expert report that none of the 6 cohort studies showed an increased risk 7 in ovarian cancer, that was an error, 8 right? Because -- 9 A. No. 10 Q. -- serous ovarian cancer is 11 a form of ovarian cancer, true? 12 MS. CURRY: Object to the 13 form. 14 THE WITNESS: No. I don't 15 see that as an error, because if I 16 have two studies of the same 17 population, one with 14 years of 18 follow-up, which you seem to take 19 a lot of issue with, and one with 20 24 years follow-up, I was under 21 impression with your criticisms of 22 the study that the one with the 23 longer follow-up would be 24 considered more accurate.</p>	<p>1 BY MS. GARBER: 2 Q. I didn't ask you why. My 3 question was very clear and precise. 4 MS. SHARKO: You can't 5 interrupt him. 6 BY MS. GARBER: 7 Q. Did you -- did you in the 8 four corners of your report state what 9 the results were for serous ovarian 10 cancer in Gertig, yes or no? 11 A. Let me take a look and see. 12 Yes, I did mention it. 13 Q. And, Doctor, do you state at 14 the top of Page 11 that the Gates 2010 15 reversed the finding of the only cohort 16 study reporting the association between 17 genital talc and epithelial ovarian 18 cancer? 19 A. Yes. 20 Q. What is your basis for that? 21 A. Pretty much as I stated in 22 the report, that you said that I didn't 23 state, is that there was a modest 24 increased risk for invasive serous</p>

Kevin Holcomb, M.D.

Page 358	Page 360
<p>1 ovarian cancer in the Gertig study, which</p> <p>2 was stated on the bottom of Page 10</p> <p>3 clearly. And that -- I can read it to</p> <p>4 you, "In 2010 Gates, et al." --</p> <p>5 Q. You don't have to read it,</p> <p>6 Doctor. I can read it for myself. Let</p> <p>7 me withdraw that.</p> <p>8 Doctor, did the Gates</p> <p>9 authors state that their study reversed</p> <p>10 the findings of the Gertig 2000 study?</p> <p>11 MS. CURRY: Object to the</p> <p>12 form.</p> <p>13 THE WITNESS: The results</p> <p>14 did, yes.</p> <p>15 BY MS. GARBER:</p> <p>16 Q. Did the study authors say</p> <p>17 our data reversed the findings, used that</p> <p>18 phrase, "reversed the findings" of the</p> <p>19 Gertig study?</p> <p>20 A. I'd have to read through the</p> <p>21 study to see if it was mentioned.</p> <p>22 Q. Is it epidemiologically</p> <p>23 sound to say, "My study reversed the</p> <p>24 findings of a prior study"?</p>	<p>1 Q. In fact, there are</p> <p>2 epidemiological studies as recent as</p> <p>3 2018, that use the Gertig study in their</p> <p>4 meta-analysis, right, the Penninkilampi</p> <p>5 for one?</p> <p>6 A. That is true. And a</p> <p>7 weakness of the study.</p> <p>8 Q. We're going to get to that.</p> <p>9 I'm sure that's your opinion. But that</p> <p>10 study relies on the Gertig study, in</p> <p>11 other words, if they are including it in</p> <p>12 their meta-analysis, surely those study</p> <p>13 authors aren't thinking that the results</p> <p>14 are reversed by Gates, correct?</p> <p>15 A. And --</p> <p>16 MS. CURRY: Object to the</p> <p>17 form.</p> <p>18 THE WITNESS: -- and by not</p> <p>19 including Gates, they will come to</p> <p>20 a spurious result. They will</p> <p>21 think that maybe a prospective</p> <p>22 study supports that there's an</p> <p>23 increased risk. Where if they had</p> <p>24 done -- and this is what I was</p>
Page 359	Page 361
<p>1 MS. CURRY: Object to the</p> <p>2 form.</p> <p>3 BY MS. GARBER:</p> <p>4 Q. Have you ever heard that</p> <p>5 done?</p> <p>6 A. I use the term. So yes,</p> <p>7 I've heard it done.</p> <p>8 Q. It's your turn -- it's your</p> <p>9 term?</p> <p>10 MS. CURRY: Object to the</p> <p>11 form.</p> <p>12 THE WITNESS: I use it in my</p> <p>13 report, yes.</p> <p>14 BY MS. GARBER:</p> <p>15 Q. Have you seen any other</p> <p>16 study authors who say, in all of</p> <p>17 epidemiological literature that you've</p> <p>18 looked at, that says that the Gates 2010</p> <p>19 study reversed the findings of the Gertig</p> <p>20 2000 study?</p> <p>21 A. I could not tell you that</p> <p>22 out of all the epidemiologic studies that</p> <p>23 I've read whether or not that term was</p> <p>24 used.</p>	<p>1 saying about meta-analysis.</p> <p>2 Not only do you have to</p> <p>3 worry about heterogeneity. And we</p> <p>4 spent enough time talking about</p> <p>5 that. But selection of the</p> <p>6 studies that go into your</p> <p>7 meta-analysis are very, very</p> <p>8 important. And one -- and</p> <p>9 selection bias is -- is a very</p> <p>10 important thing that you have to</p> <p>11 watch out for as well.</p> <p>12 So the fact that</p> <p>13 Penninkilampi, as late as that</p> <p>14 study just came out, was unable to</p> <p>15 figure out that that same cohort</p> <p>16 had been followed for ten years</p> <p>17 longer, we -- strengthening the</p> <p>18 study by increasing the follow-up</p> <p>19 time, all the criticisms you just</p> <p>20 gave me about Gertig is now</p> <p>21 strengthened in Gates, and yet you</p> <p>22 choose to use the number from</p> <p>23 Gertig. I'd have to ask why would</p> <p>24 somebody who's seeking the truth</p>

Kevin Holcomb, M.D.

<p style="text-align: right;">Page 362</p> <p>1 do that.</p> <p>2 BY MS. GARBER:</p> <p>3 Q. I'm going to show you some</p> <p>4 data and see if we can figure that out</p> <p>5 together.</p> <p>6 You don't have any basis to</p> <p>7 conclude that the Penninkilampi authors</p> <p>8 didn't know about the Gates 2010 data,</p> <p>9 did you?</p> <p>10 MS. CURRY: Object to the</p> <p>11 form.</p> <p>12 THE WITNESS: I'm saying</p> <p>13 that I don't see in their</p> <p>14 definitions, including the studies</p> <p>15 that they included, the search</p> <p>16 terms that they included, a reason</p> <p>17 why they would negate Gates.</p> <p>18 BY MS. GARBER:</p> <p>19 Q. Do you know whether or not</p> <p>20 the Taher authors included the Gertig or</p> <p>21 the Gates study?</p> <p>22 A. I believe they included</p> <p>23 both. But if I can look at it. Because</p> <p>24 earlier that was where I was telling you</p>	<p style="text-align: right;">Page 364</p> <p>1 A. Correct.</p> <p>2 Q. And the age of the women in</p> <p>3 the Gates 2010 were younger than the</p> <p>4 study women in the Gertig?</p> <p>5 MS. CURRY: Objection to</p> <p>6 form.</p> <p>7 BY MS. GARBER:</p> <p>8 Q. Is that true?</p> <p>9 A. I'm sorry, say the --</p> <p>10 Q. Sorry. The age of the women</p> <p>11 in Gates 2010 were younger than the</p> <p>12 Gertig women, correct?</p> <p>13 MS. CURRY: Object to form.</p> <p>14 THE WITNESS: You mean the</p> <p>15 same women that were followed</p> <p>16 in -- in Gertig, by the time they</p> <p>17 saw them ten years later they were</p> <p>18 younger?</p> <p>19 BY MS. GARBER:</p> <p>20 Q. Is there a disparity in the</p> <p>21 age of the two cohorts?</p> <p>22 A. Between Gertig and Gates.</p> <p>23 MS. CURRY: Not -- I</p> <p>24 think --</p>
<p style="text-align: right;">Page 363</p> <p>1 that they are saying Gates shows a</p> <p>2 possible increased risk of cancer in</p> <p>3 their table, where -- and I'm talking</p> <p>4 about on the -- the -- can I pull out</p> <p>5 Taher since you bring it up?</p> <p>6 Q. That's okay. We're going</p> <p>7 to -- we're going to get there in a</p> <p>8 minute --</p> <p>9 A. Okay.</p> <p>10 Q. -- when I'm done with these</p> <p>11 cohorts, so...</p> <p>12 All right. Let's -- let's</p> <p>13 talk about Gates 2010.</p> <p>14 (Document marked for</p> <p>15 identification as Exhibit</p> <p>16 Holcomb-20.)</p> <p>17 BY MS. GARBER:</p> <p>18 Q. I'll mark as Exhibit 20, the</p> <p>19 Gates 2010 publication:</p> <p>20 Doctor, the Gates 2010</p> <p>21 article was a publication of the</p> <p>22 follow-up to the Nurses' Health Study I</p> <p>23 that was published as Gertig in the year</p> <p>24 2000, correct?</p>	<p style="text-align: right;">Page 365</p> <p>1 THE WITNESS: I'm a -- I'm a</p> <p>2 little confused by your question.</p> <p>3 BY MS. GARBER:</p> <p>4 Q. Okay. Do you understand</p> <p>5 that the women who were included in the</p> <p>6 Gates study were younger than the women</p> <p>7 in the Gertig study?</p> <p>8 MS. CURRY: Object to the</p> <p>9 form.</p> <p>10 BY MS. GARBER:</p> <p>11 Q. Maybe I'll show you --</p> <p>12 A. Yes.</p> <p>13 Q. -- and then you can maybe</p> <p>14 help me understand.</p> <p>15 A. Because I don't need to read</p> <p>16 through.</p> <p>17 Q. Doctor, if you could look</p> <p>18 right here?</p> <p>19 A. Sure.</p> <p>20 Q. On the first page. Do you</p> <p>21 see where it says, "The Nurses' Health</p> <p>22 Study was established in 1976 and the</p> <p>23 Nurses' Health Study II in 1989 amongst</p> <p>24 121,700 U.S. women" -- "U.S. female</p>

Kevin Holcomb, M.D.

Page 366	Page 368
<p>1 registered nurses aged 30 to 55 and 2 116,430 U.S. female registered nurses 3 aged 25 to 42 respectively." 4 So the two cohorts are 5 different ages, are they not? 6 MS. CURRY: Object to the 7 form. 8 THE WITNESS: I'm sorry, I'm 9 just taking my time to read 10 through this again. 11 BY MS. GARBER: 12 Q. Mm-hmm. Do you need time to 13 study? We'll go off the record if you 14 do. 15 A. No. That seems to be the 16 case, yes. 17 Q. Okay. Okay. In the Gates 18 study they were not asked questions about 19 it -- about their talc use. Instead, the 20 data about their talc exposure was 21 carried over from the Gertig one-time 22 1982 questionnaire. Do you agree with 23 that? 24 A. It's my understanding that</p>	<p>1 the metric is talc use greater than once 2 a week versus less than once a week. 3 It's not ever never, correct? 4 A. Correct. 5 Q. That's a different metric 6 from Gertig, right? 7 A. Different metric, yes. 8 Q. Thank you. 9 A. Valid -- valid change 10 though. 11 Q. Okay. But different 12 nonetheless, right? 13 A. Different and valid. 14 Q. While the Gates 2010 study 15 followed women for ten more years, the 16 follow-up is, in total, 26 years, 17 correct? 18 A. Correct. 19 Q. And we don't know when the 20 women were exposed, at what age they 21 began using talc, correct, the study 22 doesn't -- either study doesn't tell us 23 that, correct? 24 A. No.</p>
Page 367	Page 369
<p>1 the NHSII population was not queried on 2 their use of talc because it was a 3 one-time questionnaire in 1982. 4 So yes, the NHSII 5 population is younger than the NHSI, but 6 the question of the effect of talc on 7 ovarian cancer was in -- only in patients 8 that have been asked about ovarian cancer 9 exposure. 10 Q. Mm-hmm. And that's a study 11 limitation, correct? 12 A. No. 13 Q. Okay. In the Gates 2010 the 14 authors provide no results for ever use 15 of talcum powder product on the perineum 16 for ovarian cancer; is that true? 17 A. No. 18 Q. It's not true? 19 A. No. Hold on one second. 20 Sorry. I have to go and find. 21 Q. Doctor, if you turn to 22 Table 4 -- 23 A. Yes. 24 Q. -- Page 50. You see that</p>	<p>1 Q. And assuming the latency for 2 ovarian cancer is 30 to 40 years, that 3 study period would be inadequate to 4 accurately detect all of the women with 5 ovarian cancer. Would you agree with 6 that? 7 MS. CURRY: Object to the 8 form. 9 THE WITNESS: No. I think 10 if you -- if you can stretch to 11 the assumption that the latency 12 for something that's not even 13 proven carcinogenic is the same as 14 somebody working in a gas mask 15 factory, I think you can 16 equally -- in fact, it takes less 17 of a stretch to believe that the 18 women didn't start talc use four 19 years before they went on the 20 study, because that is not what 21 most people believe, even 22 Dr. Cramer doesn't believe most 23 women start that late in life. 24 BY MS. GARBER:</p>

Kevin Holcomb, M.D.

Page 370	Page 372
<p>1 Q. But you have no data as to 2 when the women in this study actually 3 started talc use, do you? 4 A. No. 5 Q. The Gates relative risk for 6 women who use talc greater than once a 7 week and serous ovarian cancer is 1.06 8 with a confidence interval of 0.84 to 9 1.35. Do you agree with that? 10 A. Sorry, one second. Yes. 11 Q. And again, under your 12 definition of positive, you do not think 13 that is a positive finding, correct? 14 A. Positive and not 15 statistically significant, yes. 16 Q. You do think it's positive, 17 but not statistically significant? 18 MS. CURRY: Object to the 19 form. 20 THE WITNESS: If you're 21 asking me about directionality, 22 it's obvious. Because 23 directionality it's positive. 24 I do not consider it a</p>	<p>1 directionality. And that's why I said 2 it's obviously directionality positive. 3 And if you're asking me is 4 it a valid study, one that I would rely 5 on with a degree of medical certainty, I 6 would say no, because I'm one of those 7 old school doctors who still believe that 8 95 percent confidence intervals are 9 important. 10 Q. If the Court asked you if 11 the Gertig serous ovarian cancer in the 12 Gates study was positive or negative, how 13 would you reply? 14 A. I would say it's a negative. 15 Q. Okay. And I think we 16 already covered this. But you can't cite 17 me to any authority, can you, that the 18 Gates study reverses the Gertig finding, 19 correct? 20 MS. CURRY: Object to the 21 form. 22 THE WITNESS: Well, I'm here 23 giving my testimony. So I'm going 24 to assume the mantle of an</p>
Page 371	Page 373
<p>1 significant or valid finding 2 because I can't say for 90 3 percent, 95 percent accuracy, that 4 the true risk estimate lies above 5 one. 6 BY MS. GARBER: 7 Q. So, Doctor, earlier today 8 you told me that where relative risk was 9 greater than one, but not statistically 10 significant, that was a negative finding. 11 Are you now changing your 12 definition of positive versus negative? 13 A. I think you just misstated 14 my statement, because that's not -- 15 doesn't make sense what you just said. 16 Q. Okay. I thought you told me 17 earlier today when I asked you what a 18 negative study was, it included an odds 19 ratio that could be greater than one but 20 if it wasn't statistically significant, 21 it was a negative study in your opinion? 22 A. In this term, the question 23 that you just asked me when you were 24 asked positive, I thought you were asking</p>	<p>1 authority. And I would say if 2 this group is followed for ten 3 years longer -- and I'll add the 4 caveat that women who used it for 5 less than one week had the same 6 risk in a study just two years 7 before this, as women who had 8 never used. 9 So if you go to Gates 2008, 10 you will see for this study cohort 11 there's no reason to believe that 12 it's not a valid thing to lump 13 somebody who used it in less than 14 one week with never used, based on 15 the Gates 2008 data. 16 So, yes, I would say this 17 1.4 that was found in Gertig is 18 not -- is no longer here. 19 And so in my estimation, 20 this reverses the findings. This 21 says in the same population of 22 women followed longer, the 23 increased risk went away. 24 BY MS. GARBER:</p>

Kevin Holcomb, M.D.

Page 374	Page 376
<p>1 Q. The study authors, again, do 2 not say that, correct? 3 A. I'd have to -- 4 Q. They don't say it reverses? 5 A. I don't remember. I'd have 6 to read through the whole discussion 7 section for you. 8 Q. Okay. And, Doctor, as to 9 the Houghton study, the WHI study, you 10 read that one, right? 11 A. Yes. 12 Q. You say in your report, at 13 Page 11 in sort of the middle of the 14 page, that there was no statistically 15 significant association between use of 16 genital talc and the development of 17 ovarian cancer for ever users? 18 A. I'm sorry. The page again? 19 Q. Page 11. 20 A. Yes. 21 Q. And to make that statement, 22 there is -- 23 A. I'm still looking for it. 24 One second.</p>	<p>1 BY MS. GARBER: 2 Q. And what was the exposure 3 metric in the Houghton study? 4 A. There was a question at 5 baseline with, "Have you ever used powder 6 on your private parts/genital areas?" 7 And then respondents responding yes, were 8 then asked to identify the duration of 9 use. It was less than one year, one to 10 four years, five to nine years, and all 11 the way up to greater than 20 years. 12 Q. And, Doctor, that's -- 13 that's a duration of use -- 14 A. Right. 15 Q. -- assessment, right? 16 A. Yes. 17 Q. And that doesn't take into 18 consideration frequency of use, right? 19 A. No. 20 Q. All right. And then the 21 Houghton authors state that the Nurses' 22 Health Study found that there was a 23 40 percent increase in the risk with a 24 confidence interval of 1.02 to 1.91?</p>
Page 375	Page 377
<p>1 Q. It's in the middle of the 2 page. 3 A. Can you repeat the statement 4 that you said I'm looking for. 5 Q. In your expert report at 6 Page 11 as to the Houghton study -- 7 A. Yes. 8 Q. -- you indicate that there 9 was no statistically significant 10 association. 11 A. I'm looking for the term 12 that you're saying. 13 Q. That's okay, Doctor. 14 Do you know what the sample 15 size was in the WHI study? 16 A. I think it was about 61,000. 17 Q. And based on the relative 18 small size, that's a study limitation of 19 the Houghton study, correct? 20 MS. CURRY: Object to the 21 form. 22 THE WITNESS: As taken in a 23 vacuum as an individual study, 24 yes.</p>	<p>1 A. I'm not sure where you're 2 looking. 3 Q. Okay. Doctor, if you look 4 at the right-hand -- yeah. If you look 5 at the first page, the right-hand column. 6 MS. CURRY: Which study? 7 Sorry. 8 MS. GARBER: Houghton. 9 THE WITNESS: Yeah, but we 10 don't -- 11 MS. CURRY: You haven't 12 marked it as an exhibit. 13 MS. GARBER: Oh, I'm sorry, 14 you guys. 15 (Document marked for 16 identification as Exhibit 17 Holcomb-21.) 18 BY MS. GARBER: 19 Q. Okay. Let's mark the 20 Houghton 2014 study. Doctor, if you look 21 at the right-hand column, here. 22 MS. SHARKO: What exhibit is 23 this? 24 MS. GARBER: What?</p>

95 (Pages 374 to 377)

Kevin Holcomb, M.D.

Page 378	Page 380
<p>1 MS. CURRY: 21. 2 MS. SHARKO: Oh, 21? Okay. 3 BY MS. GARBER: 4 Q. Doctor, do you see where I'm 5 marking right here, on the right-hand 6 side? 7 A. Yes. 8 Q. The -- the sentence begins, 9 "In the Nurses' Health Study (NHS) 10 cohort, no overall association was found 11 between the use of perineal powder and 12 epithelial ovarian cancer" -- and it 13 cites the risk -- "or serous ovarian 14 cancer," and it cites the odds ratio. It 15 goes on to say, "However, there was a 16 40 percent with a 95 percent confidence 17 interval of 1.02 to 1.91 increased risk 18 for serous invasive ovarian cancer with 19 ever perineal use, which comprises 20 86 percent of the serous ovarian cancers 21 in the cohort." 22 Did I read that correctly? 23 A. You read it correctly. 24 Q. And that cites to the Gertig</p>	<p>1 date, there has only been one 2 prospective study conducted the 3 powder use and risk of ovarian 4 cancer," and then only cite 5 Gertig, which in fact to that 6 date, there had been two studies. 7 If you don't want to say one 8 reversed it. Then you have to at 9 least admit that there was two 10 studies. It was Gertig and Gates. 11 So the fact that they made that 12 mistake from the beginning of that 13 paragraph and follow it through 14 with only talking about Gertig, 15 yes, you're accurate -- you read 16 perfectly right what they said. 17 But my point is that that's not an 18 accurate statement. There was 19 more than one. 20 BY MS. GARBER: 21 Q. So Nurses' Health Study was 22 one study, right, with two publications? 23 A. No, I think that if you are 24 talking about how many studies,</p>
Page 379	Page 381
<p>1 study, right? 2 A. Yes. The beginning of that 3 paragraph says, "To date there has only 4 been one prospective study conducted." 5 This is 2013. And we've already 6 established there was a follow-up to that 7 study in 2010 that wasn't included here. 8 Q. And that's precisely my 9 point. So here, the Houghton authors are 10 citing to the Gertig study, not the Gates 11 study, correct? 12 A. That's correct. And I would 13 consider it inappropriate not to mention 14 that follow-up information. 15 Q. The authors don't say that 16 the Gates 2010 reversed the findings of 17 the Gertig study; rather, they cite those 18 data, don't they? 19 A. They do. 20 MS. CURRY: Object to the 21 form. 22 THE WITNESS: I just think 23 it's a mistake to leave out what 24 clearly -- this statement, "To</p>	<p>1 there's -- there is two different 2 publications. You're right, they are 3 only citing one of them. 4 Q. So the Nurses' Health Study 5 was one study with two publications or it 6 was two studies with two publications? 7 MS. CURRY: Object to the 8 form. 9 THE WITNESS: As you can see 10 with my case-control lists for 11 example, I still counted those as 12 separate studies and you are 13 talking about what percentage are 14 positive, what percentage are 15 negative. When, in fact, I had 16 studies that were reported on the 17 same populations at later time. I 18 can -- I considered them two 19 studies. 20 So I'm -- the Nurses' Health 21 Study was one prospective study 22 with -- with two publications. 23 And the fact that they don't cite 24 Gates, I see as a weakness to</p>

Kevin Holcomb, M.D.

Page 382	Page 384
<p>1 their -- their introduction.</p> <p>2 BY MS. GARBER:</p> <p>3 Q. You think they should have</p> <p>4 cited the Gates 2010 study?</p> <p>5 A. I think that's -- I think</p> <p>6 that's -- it should make you pause when</p> <p>7 the only prospective study that you're</p> <p>8 quoting has this increased risk. And</p> <p>9 then the women followed longer, the risk</p> <p>10 goes away. It's worth mentioning I would</p> <p>11 think.</p> <p>12 Q. Well, Doctor, the Gates</p> <p>13 study is peer reviewed and published,</p> <p>14 right?</p> <p>15 A. Yes.</p> <p>16 Q. And the Penninkilampi is</p> <p>17 peer reviewed and published, correct?</p> <p>18 A. Yes.</p> <p>19 Q. And I know the Taher isn't</p> <p>20 yet peer reviewed, but it -- it cites to</p> <p>21 the Gertig study too, doesn't it?</p> <p>22 A. Repeated --</p> <p>23 MS. CURRY: Object to the</p> <p>24 form.</p>	<p>1 A. I have to go back to the</p> <p>2 materials and methods to see if they</p> <p>3 asked. One second.</p> <p>4 No.</p> <p>5 Q. Okay. And while there is</p> <p>6 duration of exposure, you don't know how</p> <p>7 many women were exposed to long-term talc</p> <p>8 defined by more than 20 years, do you,</p> <p>9 this study doesn't report that data, does</p> <p>10 it?</p> <p>11 A. How many women had used it</p> <p>12 for 20 or more years?</p> <p>13 Q. Yes.</p> <p>14 A. I'd have to go to the</p> <p>15 results to check for that. Because it</p> <p>16 was part of the questions.</p> <p>17 Q. All right. That's all</p> <p>18 right. I'll withdraw the question.</p> <p>19 And turning to Page 4,</p> <p>20 Table 2. It shows the number of women in</p> <p>21 the study who reported using talcum</p> <p>22 powder products on their genitals, right?</p> <p>23 A. Yes.</p> <p>24 Q. And how many women used</p>
Page 383	Page 385
<p>1 THE WITNESS: -- mistakes</p> <p>2 don't make it less of a mistake.</p> <p>3 BY MS. GARBER:</p> <p>4 Q. Okay. But -- but at least</p> <p>5 the Gertig and the Penninkilampi are peer</p> <p>6 reviewed and cite --</p> <p>7 A. Some of -- so --</p> <p>8 Q. -- to Gertig --</p> <p>9 A. Yes.</p> <p>10 Q. -- is that true?</p> <p>11 A. Yes, yes.</p> <p>12 Q. Okay. Let's talk further</p> <p>13 about the Houghton study --</p> <p>14 A. Yes.</p> <p>15 Q. -- the WHI study. The study</p> <p>16 enrolled 61,576 postmenopausal women,</p> <p>17 right?</p> <p>18 A. I'm sorry --</p> <p>19 Q. It's in the abstract under</p> <p>20 results?</p> <p>21 A. Yes.</p> <p>22 Q. Okay. And you don't -- do</p> <p>23 you know when the women started using</p> <p>24 talc, at what age, in this study?</p>	<p>1 it -- let me catch up to you. How many</p> <p>2 women were reporting using ten years or</p> <p>3 more?</p> <p>4 A. 68.</p> <p>5 Q. Not very many, is it?</p> <p>6 MS. CURRY: Object to the</p> <p>7 form.</p> <p>8 THE WITNESS: No.</p> <p>9 This -- you -- let me</p> <p>10 clarify. You're asking not how</p> <p>11 many women used it for longer, but</p> <p>12 how many women who developed</p> <p>13 ovarian cancer that had used it.</p> <p>14 BY MS. GARBER:</p> <p>15 Q. Yeah.</p> <p>16 A. That's 68. Yes.</p> <p>17 Q. Yeah. It's not very many</p> <p>18 women in that study group, is it?</p> <p>19 MS. CURRY: Object to the</p> <p>20 form.</p> <p>21 THE WITNESS: Relative to?</p> <p>22 BY MS. GARBER:</p> <p>23 Q. Relative to 200,000?</p> <p>24 A. Narod didn't say you need</p>

Kevin Holcomb, M.D.

Page 386	Page 388
<p>1 200,000 women with ovarian cancer. He 2 said you need 200,000 women total. 3 Q. Okay. Is 68 who developed 4 ovarian cancer a good amount that gives 5 you confidence in these data? 6 MS. CURRY: Object to the 7 form. 8 THE WITNESS: You know, the 9 smaller the number, the wider the 10 confidence interval would be. 11 BY MS. GARBER: 12 Q. Is this a wide confidence 13 interval? You testified in the Ingham 14 case it was, didn't you? 15 A. That this is a wide 16 interval? 17 Q. Mm-hmm. 18 A. Well, it crosses -- it's 19 wide enough, and it's in the wrong -- you 20 know, it crosses one, so it's not 21 statistically significant. 22 So that apparent reduction 23 in the risk, that 2 percent reduction in 24 the risk, I wouldn't trust it.</p>	<p>1 BY MS. GARBER: 2 Q. Okay. Another limitation of 3 the study was that one-sided metric of 4 only capturing duration. Do you agree 5 with that? 6 MS. CURRY: Object to the 7 form. 8 THE WITNESS: I think a 9 perfect study would collect -- 10 collect both. So yes. 11 BY MS. GARBER: 12 Q. It would be an optimal study 13 to collect both, wouldn't it? 14 MS. CURRY: Object to the 15 form. 16 THE WITNESS: Unfortunately 17 there is no such thing as an 18 optimal study. I could look at 19 all -- every study I reviewed and 20 pick up things that should have 21 been done differently and better. 22 And hopefully learn with the next 23 study design. But that's true for 24 everything in my reliance list.</p>
Page 387	Page 389
<p>1 Q. That's a limitation of the 2 study, right, the wide confidence 3 interval, in that few women -- few number 4 of women participants? 5 MS. CURRY: Object to the 6 form. 7 BY MS. GARBER: 8 Q. Right? 9 A. The few number of women 10 participants, it's -- it's actually what, 11 61,000 women participants. 12 Q. The 68 women participants 13 calls into question the validity of this 14 subgroup analysis, doesn't it, Doctor? 15 MS. CURRY: Object to the 16 form. 17 THE WITNESS: If you're -- 18 the only analysis that was broken 19 down, you're saying the number of 20 women with ten or more years is 21 68. 22 And when you say that's low, 23 I'm not sure it's relative to 24 what.</p>	<p>1 BY MS. GARBER: 2 Q. Let's see if we can work out 3 how this would work. 4 If you only captured 5 duration of use and you said it was -- 6 you used it ten years or more, a given 7 woman could have used it once a year on 8 her anniversary for all you know, 9 correct? 10 A. Correct. 11 The -- the big problem with 12 this whole body of literature though, is 13 this concept that you have any idea of 14 the dose at the tissue level. 15 I -- if you told me you used 16 it everyday, and I'm a woman and I use it 17 everyday and you take three shakes and I 18 take one, we're really not getting to the 19 heart of dose-response. 20 And this -- this is a 21 difficulty of all this topic. It's -- 22 it's -- they are all limited. They are 23 all limited. We have no idea of the dose 24 of talc, if it's even getting to the</p>

Kevin Holcomb, M.D.

Page 390	Page 392
<p>1 ovaries, and if it's getting to the 2 ovaries from that dusting, what amount is 3 getting to the ovaries. And so we're 4 playing a pseudoscience game with 5 dose-response. 6 This isn't really 7 dose-response. Dose-response studies 8 have to do with the level of what you're 9 interested in at the tissue level. So we 10 can go through the stuff and talk about 11 these as weaknesses, but this whole body 12 of literature is weakened by the 13 inability to know. 14 I don't even know for sure 15 that it gets to the ovary from this way. 16 How much each women put into her -- 17 dusted with is -- is totally random. 18 Q. And that's what I want to 19 really get at here because you're aware 20 of data where there is talc found in the 21 ovarian tissue, both tumor and 22 non-diseased, right? 23 A. In women who report exposure 24 and women who don't report exposure.</p>	<p>1 Because even in the cases of 2 the particles that you find, I 3 have no idea how they got there. 4 There is -- there is a lot 5 of weakness just overall in this 6 whole area. 7 So I would be less bothered 8 by that if you gave me the 9 epidemiology data that showed me a 10 20-fold increase. Then I'm less 11 reliant or feel like you -- it's 12 less necessary. 13 But in this situation where 14 we've already gone through the 15 epidemiologic data earlier. And I 16 pointed out all the 17 inconsistencies, as I describe. I 18 call a 50/50 split inconsistent. 19 And now you get to this, and 20 you can point out all the 21 weaknesses. But I'm saying 22 there's weaknesses in all these 23 studies going through. 24</p>
Page 391	Page 393
<p>1 Q. Okay. And you're aware 2 of -- from your work in individual cases, 3 that there are women who report talcum 4 powder product exposure who have found 5 asbestos and talc in their ovaries, 6 correct? 7 MS. CURRY: Object to the 8 form. 9 THE WITNESS: There are 10 women who report neither of the 11 two who find particles that 12 diagnosed as talc or asbestos in 13 their ovaries. 14 So you're getting to my 15 point, is that the -- it falls 16 apart with the biologic 17 plausibility because of all these 18 weaknesses, because you can't 19 really assess dose at the tissue 20 level, because women who report 21 no -- because there isn't a good 22 correlation between reported 23 history of exposure and finding 24 the particles.</p>	<p>1 BY MS. GARBER: 2 Q. Doctor, do you think that 3 the data which shows that there is 4 asbestos and talc in ovarian tissue 5 provides a biologically plausible 6 mechanism of carcinogenicity? 7 MS. CURRY: Object to the 8 form. 9 THE WITNESS: Just the 10 presence of it in the -- 11 BY MS. GARBER: 12 Q. Yeah. 13 A. This is part of the problem 14 with this whole area. The presence -- 15 Q. Doctor, that wasn't my 16 question. 17 A. No. The presence -- 18 Q. Yes or no. 19 A. No. The presence of it does 20 not -- 21 Q. You don't think that -- 22 A. Just the mere presence of 23 the particle does not prove a causal 24 relationship.</p>

99 (Pages 390 to 393)

Kevin Holcomb, M.D.

Page 394	Page 396
<p>1 Q. And you've seen paper after 2 published paper wherein the study authors 3 who are actually studying talcum powder 4 exposure, talc product exposure and 5 ovarian cancer, are stating that there is 6 a biologically plausible mechanism, 7 correct? 8 MS. CURRY: Object to the 9 form. 10 THE WITNESS: The 11 statements of -- 12 BY MS. GARBER: 13 Q. You just disagree with them? 14 MS. CURRY: Object to the 15 form. 16 THE WITNESS: But the -- in 17 no situation, in medicine that I 18 can think of would a -- the mere 19 presence of a molecule or particle 20 or whatever in a certain organ be 21 evidence of its carcinogenicity. 22 That's not biologic 23 plausibility. 24 Just its mere presence</p>	<p>1 not just in talc. I would look at 2 that as a ridiculous situation in 3 any statement. 4 We're here and studying this 5 because people say they -- they 6 describe finding talc there. But 7 that's -- that's not the burden of 8 proof. 9 BY MS. GARBER: 10 Q. Okay. Do you think the 11 burden of proof is absolute proof that 12 the talc got there through perineal 13 dusting? 14 A. Does it matter how it got 15 there if it's a carcinogen? 16 Q. If it's a carcinogen, does 17 it matter? 18 A. It matters maybe for you, 19 because of the nature of this litigation. 20 But if talc caused cancer of 21 the ovary, I could care less how it got 22 there. I'd want to -- you know, the fact 23 that it's there is an issue. You'd be 24 able to prove that it's a carcinogen.</p>
Page 395	Page 397
<p>1 isn't. 2 And the fact -- the fact 3 that so many people are saying 4 that is exactly what I'm talking 5 about when people overstate the 6 findings of their studies, just 7 the -- just the finding it there 8 in no way implies biologic 9 plausibility. 10 BY MS. GARBER: 11 Q. That's your opinion, right? 12 A. That's like saying -- 13 Q. There are study authors who 14 disagree with you, correct? 15 MS. CURRY: Object to the 16 form. 17 THE WITNESS: Just to give 18 you an example, it was -- it would 19 be like saying because I went to 20 the bank, there's a plausible 21 evidence that I robbed the bank 22 because I was there. I mean, that 23 doesn't make any sense to me. 24 That's not the way I look at it,</p>	<p>1 So even the cases, the 2 Heller study, you mentioned it earlier, 3 24 women, 12 reporting a history of 4 exposure, 12 not reporting a history of 5 exposure. Not only is there not a 6 correlation, if I go back and I read the 7 paper, I think the fiber counts are even 8 higher in the women without a reported 9 history. 10 Q. We're going to look at that 11 paper in a minute. But, Doctor, don't 12 the authors suggest why that is, why the 13 unexposed group may have high fiber 14 counts? 15 MS. CURRY: Object to the 16 form. 17 THE WITNESS: Do they 18 what -- what it is? Can you 19 repeat? 20 BY MS. GARBER: 21 Q. Don't the study authors 22 suggest -- 23 A. See -- 24 Q. -- what may account for that</p>

100 (Pages 394 to 397)

Kevin Holcomb, M.D.

Page 398	Page 400
<p>1 high fiber burden in the non-exposed 2 group? 3 MS. CURRY: Object to the 4 form. 5 THE WITNESS: If you 6 equal -- if you think and suggest 7 and hypothesize are the same, I 8 would agree with you. You see 9 suggestion in science means 10 there's some evidence to make you 11 think this is the case. 12 Otherwise, you're just -- it's 13 conjecture and it's hypothesis. 14 BY MS. GARBER: 15 Q. And you read the Cramer 16 paper. Didn't the Cramer paper suggest 17 that -- address the issues, the 18 shortcomings of the Heller data, that 19 there may be surface contamination that 20 goes in and mixes with the talc or 21 asbestos in the tissue which accounts for 22 the unexposed group? 23 MS. CURRY: Object to the 24 form.</p>	<p>1 Q. No, from the paraffin 2 processing, right? 3 MS. CURRY: Object to the 4 form. 5 THE WITNESS: Contamination 6 at some point. I mean, is it 7 contamination during processing? 8 Is it from surgical gloves from 9 past surgeries? Is it from -- my 10 point is, this is all conjecture 11 because there's all these possible 12 explanations. And people can 13 suggest what they want in their 14 introduction to their paper. 15 But I'm more interested in 16 the actual science that goes to 17 the heart of trying to figure 18 out -- you know. 19 But again, you're -- we 20 started this conversation by 21 talking about the mere presence of 22 talc particles in the ovary. 23 BY MS. GARBER: 24 Q. Okay. So we'll get back to</p>
Page 399	Page 401
<p>1 BY MS. GARBER: 2 Q. Don't they suggest that? 3 A. Yes. You're saying that one 4 author says it's from one explanation and 5 Cramer says it's from another 6 explanation, so yeah, they're all 7 suggesting these different things. One 8 person saying it is diapering as a child. 9 The next person is saying it's 10 contamination. The truth is no one 11 knows. 12 Q. Did Cramer say it's coming 13 from contamination, or did Cramer say 14 that you need to do polarized light to 15 make sure that you're adequately counting 16 what's really deeply embedded in the 17 tissue and not what's coming in the 18 surface? 19 MS. CURRY: Object to the 20 form. 21 THE WITNESS: Because he 22 thinks what's on the surface is 23 contamination. 24 BY MS. GARBER:</p>	<p>1 the cohorts, and then we'll move onto the 2 biologic plausibility. 3 But you would agree with me, 4 wouldn't you, that there are study -- 5 peer-reviewed study authors that set 6 forth that there is a biologically 7 plausible mechanism. You just disagree 8 with that, correct? 9 MS. CURRY: Object to the 10 form. 11 THE WITNESS: The reason 12 that I have to disagree with it 13 is -- 14 BY MS. GARBER: 15 Q. Doctor, my question is yes 16 or no. 17 A. I disagree with it that 18 there's -- it's conjecture. 19 Q. That's fine. I understand 20 your opinion. 21 I just want you to answer my 22 question, which is you agree that there 23 are study authors that say there's 24 biologically plausible mechanism, you</p>

101 (Pages 398 to 401)

Kevin Holcomb, M.D.

Page 402	Page 404
<p>1 just disagree with that?</p> <p>2 MS. CURRY: Object to the</p> <p>3 form.</p> <p>4 BY MS. GARBER:</p> <p>5 Q. Correct?</p> <p>6 A. I disagree with it. Many</p> <p>7 people disagree with it.</p> <p>8 Q. Okay. And there's many</p> <p>9 people who agree with it, right?</p> <p>10 MS. CURRY: Object to the</p> <p>11 form.</p> <p>12 THE WITNESS: Based on</p> <p>13 pseudoscience.</p> <p>14 BY MS. GARBER:</p> <p>15 Q. Is the Health Canada</p> <p>16 pseudoscience?</p> <p>17 A. No, I wouldn't describe</p> <p>18 Health Canada as pseudoscience in</p> <p>19 totality. But if you -- if you want to</p> <p>20 read through it and ask what things I</p> <p>21 agree with and what things I don't, I</p> <p>22 think I've already told you that when --</p> <p>23 when authors make statements in their</p> <p>24 preambles, in their introductions, that</p>	<p>1 Q. Doctor, this study involved</p> <p>2 only 41,654 women, correct?</p> <p>3 A. 41,000 women, and 600.</p> <p>4 Q. Yeah. And the talc exposure</p> <p>5 metric was to ask women about the</p> <p>6 frequency of their talcum powder exposure</p> <p>7 within -- in their genitals within the</p> <p>8 prior 12 months, correct?</p> <p>9 A. Let me just confirm that.</p> <p>10 Q. It's under the methods on</p> <p>11 the abstract, Doctor.</p> <p>12 A. Can you repeat your</p> <p>13 statement just now?</p> <p>14 Q. Doctor, was one of the</p> <p>15 limitations that the -- the exposure was</p> <p>16 talcum powder exposure to the genitals</p> <p>17 within the prior 12 months. Do you agree</p> <p>18 with that?</p> <p>19 A. Yes. Along -- along with</p> <p>20 frequency. I -- I thought you were --</p> <p>21 yes.</p> <p>22 Q. Okay. And the follow-up</p> <p>23 there in the abstract was 6.6 years,</p> <p>24 right?</p>
Page 403	Page 405
<p>1 aren't based on data but they state it as</p> <p>2 a fact, watch out for what's coming</p> <p>3 later.</p> <p>4 Q. Okay. We'll go to --</p> <p>5 A. If somebody starts off like</p> <p>6 that.</p> <p>7 Q. We'll go to Health Canada</p> <p>8 and see what they said about biologic</p> <p>9 plausibility.</p> <p>10 A. You spend a lot of time in</p> <p>11 Canada.</p> <p>12 Q. You also reviewed the Gertig</p> <p>13 study, correct?</p> <p>14 A. The same study that we were</p> <p>15 just going through?</p> <p>16 Q. I'm sorry, I -- I misspoke.</p> <p>17 The Gonzalez study?</p> <p>18 A. Yes, I did.</p> <p>19 Q. And I'll mark that as</p> <p>20 Exhibit 22.</p> <p>21 (Document marked for</p> <p>22 identification as Exhibit</p> <p>23 Holcomb-22.)</p> <p>24 BY MS. GARBER:</p>	<p>1 A. Yes.</p> <p>2 Q. And you don't know when the</p> <p>3 women started using talc, right?</p> <p>4 A. No.</p> <p>5 Q. Like the others?</p> <p>6 A. As I -- I would anticipate</p> <p>7 that they were average users.</p> <p>8 Q. Doctor, does douching</p> <p>9 increase the risk for ovarian cancer?</p> <p>10 A. This study suggests it does.</p> <p>11 Q. Is douching a risk factor</p> <p>12 for ovarian cancer?</p> <p>13 A. This study suggests it is.</p> <p>14 Q. Do you tell your patients</p> <p>15 that douching is a risk factor for</p> <p>16 ovarian cancer?</p> <p>17 A. No. Because it's only one</p> <p>18 study suggesting it.</p> <p>19 Q. And, Doctor, any of the</p> <p>20 limitations that we've just gone through</p> <p>21 with regard to the cohort studies, none</p> <p>22 of them are listed within the four</p> <p>23 corners of your expert report; is that</p> <p>24 correct?</p>

102 (Pages 402 to 405)

Kevin Holcomb, M.D.

<p style="text-align: right;">Page 406</p> <p>1 MS. CURRY: Object to the</p> <p>2 form.</p> <p>3 THE WITNESS: The</p> <p>4 limitations of cohort studies in</p> <p>5 general?</p> <p>6 BY MS. GARBER:</p> <p>7 Q. That we've gone through</p> <p>8 here, as we've gone through the cohorts.</p> <p>9 A. The --</p> <p>10 Q. You have not -- you have not</p> <p>11 put forth in the four corners of your</p> <p>12 report any of the study limitations of</p> <p>13 the cohorts, correct?</p> <p>14 A. I'd have to read through</p> <p>15 the -- through this again. I -- I don't</p> <p>16 remember exactly, you know, every word</p> <p>17 that I said about them.</p> <p>18 Q. Doctor, let's talk about the</p> <p>19 meta-analyses.</p> <p>20 A. Sure.</p> <p>21 (Document marked for</p> <p>22 identification as Exhibit</p> <p>23 Holcomb-23.)</p> <p>24 BY MS. GARBER:</p>	<p style="text-align: right;">Page 408</p> <p>1 MS. CURRY: Do you have</p> <p>2 copies of that?</p> <p>3 BY MS. GARBER:</p> <p>4 Q. Doctor, what I've attempted</p> <p>5 to do is to show the results for talcum</p> <p>6 powder product and ovarian cancer results</p> <p>7 of the meta-analyses.</p> <p>8 A. Mm-hmm.</p> <p>9 Q. And I've listed there the</p> <p>10 meta-analyses and the pooled study.</p> <p>11 The -- as you see study type, the Berge</p> <p>12 study indicates it's a pooled study.</p> <p>13 All of those odds ratios are</p> <p>14 within the vicinity of 1.22 to 1.35.</p> <p>15 Do you see that?</p> <p>16 A. Yes.</p> <p>17 MS. CURRY: Object to the</p> <p>18 form.</p> <p>19 BY MS. GARBER:</p> <p>20 Q. And those are discrepant</p> <p>21 results?</p> <p>22 A. I wasn't speaking about the</p> <p>23 strength of association. I think you</p> <p>24 assumed that.</p>
<p style="text-align: right;">Page 407</p> <p>1 Q. I'm going to mark the</p> <p>2 Penninkilampi paper. Exhibit 23.</p> <p>3 Doctor, before we turn to</p> <p>4 the Penninkilampi paper. In your expert</p> <p>5 report, you indicate that the</p> <p>6 meta-analyses -- the results of the</p> <p>7 meta-analyses --</p> <p>8 A. Can you tell me what page</p> <p>9 you are reading from?</p> <p>10 Q. Page 13.</p> <p>11 -- are discrepant. Do you</p> <p>12 recall using that phrase or that term?</p> <p>13 It's the very last two words</p> <p>14 of the first paragraph at Page 13.</p> <p>15 Do you see that?</p> <p>16 A. Yes.</p> <p>17 (Document marked for</p> <p>18 identification as Exhibit</p> <p>19 Holcomb-24.)</p> <p>20 BY MS. GARBER:</p> <p>21 Q. And I'm going to mark as</p> <p>22 Exhibit 24, a document which I will</p> <p>23 represent to you I created. It may have</p> <p>24 errors on it. I hope it doesn't.</p>	<p style="text-align: right;">Page 409</p> <p>1 I was referring to, there's</p> <p>2 discrepancies between what tumors were</p> <p>3 increased and which ones weren't. For</p> <p>4 example, Penninkilampi, I believe, found</p> <p>5 serous and endometrioid but not mucinous</p> <p>6 or clear cell. Berge found serous only.</p> <p>7 Terry found -- I don't even think Terry</p> <p>8 broke it down by...</p> <p>9 So there's discrepancies in</p> <p>10 results. I wasn't referring to the</p> <p>11 strength of association.</p> <p>12 Q. Okay.</p> <p>13 A. We spent a fair amount of</p> <p>14 time earlier talking about the levels of</p> <p>15 overlap in some of the meta-analyses.</p> <p>16 Q. We're going to give you a</p> <p>17 chance to talk about those in a second,</p> <p>18 Doctor.</p> <p>19 A. Sure.</p> <p>20 Q. With regard to talcum powder</p> <p>21 products and serous ovarian cancer in the</p> <p>22 meta-analyses, the Taher paper, the</p> <p>23 Penninkilampi paper and the Berge paper</p> <p>24 are all within 1.24 to 1.38. Do you</p>

Kevin Holcomb, M.D.

Page 410	Page 412
<p>1 agree with that?</p> <p>2 A. Can we talk -- we spoke</p> <p>3 earlier about the overlap in the number,</p> <p>4 the studies on these three studies --</p> <p>5 Q. Doctor, I --</p> <p>6 A. -- so it would be strange</p> <p>7 for the same study design to come out</p> <p>8 with discrepant results when they are</p> <p>9 looking at largely the same studies.</p> <p>10 So yes, the -- the point</p> <p>11 that these are showing consistency is not</p> <p>12 going towards proving causality. Because</p> <p>13 you would just expect that if you</p> <p>14 subjected the same studies to this study</p> <p>15 design, you really should come up with</p> <p>16 very similar results.</p> <p>17 Q. So you agree then, Doctor,</p> <p>18 that the meta-analyses both with</p> <p>19 epithelial ovarian cancer and serous</p> <p>20 ovarian cancer are consistent, correct?</p> <p>21 MS. CURRY: Object to the</p> <p>22 form.</p> <p>23 THE WITNESS: I believe they</p> <p>24 are very similar studies.</p>	<p>1 A. It's a mistake then that's</p> <p>2 not only made by Penninkilampi.</p> <p>3 Q. Right. The -- you have not</p> <p>4 performed a meta-analysis yourself, have</p> <p>5 you?</p> <p>6 A. No, I have not.</p> <p>7 Q. And you certainly do not</p> <p>8 have any evidence, do you, Dr. Holcomb,</p> <p>9 that would support your contention that</p> <p>10 if the study authors had used Gates 2010</p> <p>11 instead of Gertig, it would have changed</p> <p>12 the outcome?</p> <p>13 MS. CURRY: Object to the</p> <p>14 form.</p> <p>15 THE WITNESS: I'm not so</p> <p>16 sure about that.</p> <p>17 BY MS. GARBER:</p> <p>18 Q. You would be speculating,</p> <p>19 wouldn't you, because you haven't done</p> <p>20 that study, right?</p> <p>21 MS. CURRY: Object to the</p> <p>22 form.</p> <p>23 THE WITNESS: But that</p> <p>24 wasn't your question. Can you</p>
Page 411	Page 413
<p>1 BY MS. GARBER:</p> <p>2 Q. Is the answer to my question</p> <p>3 yes?</p> <p>4 A. Yes. I believe that when</p> <p>5 you examine the same studies you will get</p> <p>6 very similar answers.</p> <p>7 Q. With regard to your</p> <p>8 criticisms of the Penninkilampi paper,</p> <p>9 did you write the journal voicing your</p> <p>10 concerns about this study?</p> <p>11 A. No.</p> <p>12 Q. Did you attempt to contact</p> <p>13 the study authors?</p> <p>14 A. No.</p> <p>15 Q. And you indicate in your</p> <p>16 expert report that the study authors in</p> <p>17 Penninkilampi should have included the</p> <p>18 Gates study instead of the Gertig 2000</p> <p>19 study; is that correct?</p> <p>20 A. Yes.</p> <p>21 Q. And there are other study</p> <p>22 authors that we've seen that have</p> <p>23 included Gertig rather than Gates 2010,</p> <p>24 correct?</p>	<p>1 repeat your question?</p> <p>2 BY MS. GARBER:</p> <p>3 Q. Sure. I'll ask it this way.</p> <p>4 A. No, I wanted you to repeat,</p> <p>5 because I -- you're saying speculation,</p> <p>6 but I believe you asked me to speculate.</p> <p>7 Q. Sure. I'll ask you a better</p> <p>8 question.</p> <p>9 You have not performed a</p> <p>10 meta-analysis using the Gates rather than</p> <p>11 the Gertig for the ever use with</p> <p>12 epithelial ovarian cancer, true?</p> <p>13 A. As I stated earlier I have</p> <p>14 not performed any meta-analysis, so that</p> <p>15 would be true for that specific question</p> <p>16 as well.</p> <p>17 Q. And there are no study</p> <p>18 authors that have indicated it's a</p> <p>19 mistake to include Gertig rather than</p> <p>20 Gates 2010, correct?</p> <p>21 MS. CURRY: Object to the</p> <p>22 form.</p> <p>23 BY MS. GARBER:</p> <p>24 Q. In other words, Health</p>

104 (Pages 410 to 413)

Kevin Holcomb, M.D.

Page 414	Page 416
<p>1 Canada didn't say that, did they?</p> <p>2 A. Health Canada included</p> <p>3 Gates, so they didn't make the mistake.</p> <p>4 Q. But they didn't say it was a</p> <p>5 mistake for other study authors to</p> <p>6 include --</p> <p>7 A. The fact that they didn't</p> <p>8 make the same mistake, I've got to</p> <p>9 believe that they thought it was</p> <p>10 worthwhile to include the study. So yes,</p> <p>11 they thought it was a mistake not to</p> <p>12 include it. They included it.</p> <p>13 Q. Well, they didn't say it was</p> <p>14 a mistake, did they?</p> <p>15 A. Because they did it. Why</p> <p>16 would they --</p> <p>17 Q. Doctor, you are speculating,</p> <p>18 aren't you?</p> <p>19 MS. CURRY: Object to the</p> <p>20 form.</p> <p>21 BY MS. GARBER:</p> <p>22 Q. As -- as we talked about</p> <p>23 earlier --</p> <p>24 MS. SHARKO: Was that a</p>	<p>1 am?</p> <p>2 A. I'm looking at A, yes.</p> <p>3 Q. Yeah, okay. Very good. And</p> <p>4 with the legend below, it indicates that</p> <p>5 2-A is any perineal talc use, right?</p> <p>6 That's a ever/never metric, right?</p> <p>7 A. That's what they say down</p> <p>8 here, yes.</p> <p>9 Q. Right. And as we see, Gates</p> <p>10 is not an ever/never, is it?</p> <p>11 A. Neither is Wu, et al., 2015</p> <p>12 and they included that --</p> <p>13 Q. I thought you might say</p> <p>14 that. Let's look at Wu. Or let's look</p> <p>15 at what Penninkilampi says about Wu.</p> <p>16 A. Okay.</p> <p>17 Q. Let's go to Page 43 of the</p> <p>18 Penninkilampi paper. And here in the</p> <p>19 middle of the paragraph.</p> <p>20 Do you see where I am?</p> <p>21 A. Yes.</p> <p>22 Q. It says, "Note that the Wu,</p> <p>23 et al., 2015 include results from Wu</p> <p>24 2009. However, only Wu, et al., 2009,</p>
Page 415	Page 417
<p>1 question the doctor should answer?</p> <p>2 BY MS. GARBER:</p> <p>3 Q. Did you answer my question?</p> <p>4 A. I'm a little confused if you</p> <p>5 can repeat.</p> <p>6 Q. I'll just withdraw and move</p> <p>7 on.</p> <p>8 Doctor, the exposure for</p> <p>9 Gertig was ever/never, right?</p> <p>10 A. Right.</p> <p>11 Q. And the exposure for Gates</p> <p>12 was not ever/never, was it?</p> <p>13 A. No.</p> <p>14 Q. And so let's look at</p> <p>15 Penninkilampi, if we could. Page 46,</p> <p>16 figure A.</p> <p>17 Do you see where I am?</p> <p>18 Figure 2-A.</p> <p>19 A. I'm sorry, 2-A? I'm looking</p> <p>20 at -- oh, I'm looking at Table 2. 46.</p> <p>21 Sorry.</p> <p>22 Q. It's on Page 46.</p> <p>23 A. Yes.</p> <p>24 Q. And -- do you see where I</p>	<p>1 reported on non-perineal talc use total</p> <p>2 lifetime applications and long-term talc</p> <p>3 use, hence data were extracted from Wu</p> <p>4 2015 for any perineal use outcome from</p> <p>5 the Wu, et al., 2009, for the" -- "for</p> <p>6 the three other outcomes previously</p> <p>7 mentioned."</p> <p>8 So the authors in</p> <p>9 Penninkilampi were trying to keep the</p> <p>10 data consistent and keep with ever/never</p> <p>11 exposure, not change the metric, right,</p> <p>12 Doctor?</p> <p>13 A. Give me one -- give me one</p> <p>14 second just read that. Note that Wu, et</p> <p>15 al...</p> <p>16 MS. CURRY: Object to the</p> <p>17 form. And do you have a copy of</p> <p>18 Wu 2015? Do you have a copy of</p> <p>19 the Wu 2015 paper?</p> <p>20 MS. GARBER: I may. I don't</p> <p>21 know if I'm going to use it. You</p> <p>22 can if you'd like.</p> <p>23 BY MS. GARBER:</p> <p>24 Q. Doctor, should we go off the</p>

Kevin Holcomb, M.D.

<p style="text-align: right;">Page 418</p> <p>1 record while you read that?</p> <p>2 A. Well, I guess I don't -- I'm</p> <p>3 trying to figure out, is he saying that</p> <p>4 he only looked at the patients in Wu 2015</p> <p>5 that were actually included in the Wu</p> <p>6 2009 for that --</p> <p>7 Q. Doctor, if you don't</p> <p>8 understand what the authors are saying --</p> <p>9 A. I don't.</p> <p>10 Q. -- we'll just move on.</p> <p>11 A. Yeah, I don't understand.</p> <p>12 Q. Okay. All right. Let's</p> <p>13 move on.</p> <p>14 A. Because it seems to me that</p> <p>15 he would only include Wu 2009.</p> <p>16 Q. Doctor, I don't have a</p> <p>17 question pending.</p> <p>18 A. If Wu 2009 only had the ever</p> <p>19 use, why have Wu 2015 cited if you only</p> <p>20 used the patients on 2009?</p> <p>21 MS. GARBER: Objection to</p> <p>22 strike as nonresponsive.</p> <p>23 BY MS. GARBER:</p> <p>24 Q. Doctor, I did not have a</p>	<p style="text-align: right;">Page 420</p> <p>1 they were similar to IARC,</p> <p>2 possibly a carcinogen.</p> <p>3 BY MS. GARBER:</p> <p>4 Q. Health Canada?</p> <p>5 A. Yes.</p> <p>6 Q. Okay. Let's look at Health</p> <p>7 Canada.</p> <p>8 A. Sure. I have it open.</p> <p>9 Q. Doctor, if you can turn to</p> <p>10 Page 21, and right above 6.2, exposure</p> <p>11 assessment, it indicates, "The most</p> <p>12 recent meta-analysis detailed above,</p> <p>13 Taher 2018, and consistent with the Hill</p> <p>14 criteria suggest a small but consistent</p> <p>15 statistically significant positive</p> <p>16 association between ovarian cancer and</p> <p>17 perineal talc exposure. Further</p> <p>18 available data are indicative of a causal</p> <p>19 effect."</p> <p>20 Did I read that correctly?</p> <p>21 A. Yes. Apparently they</p> <p>22 disagree with IARC.</p> <p>23 Q. They looked at more data</p> <p>24 than IARC looked at, didn't they?</p>
<p style="text-align: right;">Page 419</p> <p>1 question pending.</p> <p>2 Are you aware, Doctor, that</p> <p>3 the Health Canada considered the</p> <p>4 collective meta-analyses in coming to</p> <p>5 their causal opinion regarding genital</p> <p>6 talc and risk of ovarian cancer?</p> <p>7 A. Yes.</p> <p>8 MS. CURRY: Object to the</p> <p>9 form.</p> <p>10 BY MS. GARBER:</p> <p>11 Q. And are you aware that the</p> <p>12 IARC 2010 considered the meta-analyses</p> <p>13 that were then available at the time in</p> <p>14 coming to their findings regarding talc</p> <p>15 and its carcinogenicity?</p> <p>16 A. Yes.</p> <p>17 Q. And what was Health Canada's</p> <p>18 conclusion about talc and risk of ovarian</p> <p>19 cancer? Did they come to a causal</p> <p>20 opinion?</p> <p>21 MS. CURRY: Object to the</p> <p>22 form.</p> <p>23 THE WITNESS: My memory was</p> <p>24 that they said it's possibly --</p>	<p style="text-align: right;">Page 421</p> <p>1 A. I'll tell you, I'm not -- I</p> <p>2 have to tell you that they do say causal</p> <p>3 effect here. And yet if I have time to</p> <p>4 read through this, I can show you where</p> <p>5 they say it's a possible carcinogen.</p> <p>6 And I'm not sure how you can</p> <p>7 say that something is a possible</p> <p>8 carcinogen and that it is causative of</p> <p>9 cancer in the same paper.</p> <p>10 But if you can give -- if</p> <p>11 you give me the time I can show you where</p> <p>12 it says it's a possible carcinogen.</p> <p>13 MS. GARBER: Let's take a</p> <p>14 break.</p> <p>15 THE VIDEOGRAPHER: Okay.</p> <p>16 The time -- the time is 5:01 p.m.</p> <p>17 Off the record.</p> <p>18 (Short break.)</p> <p>19 THE VIDEOGRAPHER: We are</p> <p>20 back on the record. The time is</p> <p>21 5:22 p.m.</p> <p>22 BY MS. GARBER:</p> <p>23 Q. Just so I'm clear, Doctor,</p> <p>24 it's your opinion that there is no</p>

Kevin Holcomb, M.D.

<p style="text-align: right;">Page 422</p> <p>1 biologically plausible mechanism by which 2 talc powder products can translocate or 3 migrate from the perineum to the 4 fallopian tubes and ovaries in your 5 opinion? 6 A. I want to make sure I'm 7 understanding the question. I -- there 8 is no expelling evidence that I've seen 9 that has the ability to do it. So I'm 10 not ask -- I'm not sure if you're asking 11 is it just possible or is it -- is any 12 evidence to suggest that it can happen. 13 Because if -- if you're 14 saying is it possible, I'd have to say 15 yes. If you're saying is there any 16 evidence suggesting it could happen, I 17 would have to say no. 18 Q. Doctor, is there a 19 biologically plausible mechanism by which 20 talcum powder products can translocate 21 from the perineum to the fallopian tubes 22 and ovaries in your opinion? 23 A. I would have to say it would 24 be unlikely that -- that the female</p>	<p style="text-align: right;">Page 424</p> <p>1 can happen. 2 But people hypothesizing, 3 yes, I've seen that. 4 BY MS. GARBER: 5 Q. You've seen study authors 6 who conclude that, right? 7 A. I have seen study authors 8 who hypothesize it. You can't conclude 9 it without any studies showing it. 10 (Document marked for 11 identification as Exhibit 12 Holcomb-25.) 13 BY MS. GARBER: 14 Q. I'm going to mark as 15 Exhibit 25 a document which I'll 16 represent to you is an FDA letter dated 17 April 1st, 2014. 18 And, Doctor, this document 19 appears on your reference list, doesn't 20 it? 21 A. Yes. 22 Q. And if we could turn to 23 Page 5 in the middle of the page where 24 the --</p>
<p style="text-align: right;">Page 423</p> <p>1 genital tract, while open, for obvious 2 reasons has developed many mechanisms to 3 keep particulate matter and foreign 4 bodies from ascending into the peritoneal 5 cavity. 6 So I would say it's -- it's 7 not plausible to me. 8 Q. You've seen study data that 9 would indicate that -- strike that. 10 You have seen study authors 11 who have concluded the opposite, that 12 there is a biologically plausible 13 mechanism by which talc can -- talcum 14 powder products can translocate from the 15 perineum to the fallopian tubes and 16 ovaries, right? 17 MS. CURRY: Object to the 18 form. 19 THE WITNESS: I'm assuming 20 you -- I'm assuming you struck 21 your original question because 22 they are making the statements 23 with no data. And so no, I've 24 never seen any data suggesting it</p>	<p style="text-align: right;">Page 425</p> <p>1 A. I'm sorry, give me one 2 second. 5 -- Page 4 -- 5. Mm-hmm. 3 Q. Where -- in the middle of 4 the document where the first word is 5 while. 6 Do you see where I am? 7 A. No. I'm sorry. Can -- can 8 we use the -- 9 Q. Right here in the middle, 10 where it says while. 11 A. Give me one second, ma'am. 12 Give me one second. Yes. 13 Q. "While there exists no 14 direct proof of talc and ovarian 15 carcinogenesis, the potential for 16 particulates to migrate from the perineum 17 and vagina to the peritoneal cavity is 18 indisputable." 19 Do you agree with that? 20 A. No. This is an example of 21 what I was saying earlier. Someone 22 making a very, very strong statement. 23 Indisputable, and yet there's no studies 24 showing that perineal talc can make it to</p>

Kevin Holcomb, M.D.

<p style="text-align: right;">Page 426</p> <p>1 the ovaries. And yet Dr. Epstein is</p> <p>2 saying it's indisputable.</p> <p>3 So that's not a judgment</p> <p>4 call. That's not reasonable doctors</p> <p>5 having different opinions. That's just</p> <p>6 wrong. It can't be indisputable without</p> <p>7 a single study showing its ability.</p> <p>8 Q. You -- you disagree with FDA</p> <p>9 on the issue of migration being</p> <p>10 indisputable, correct?</p> <p>11 A. No, I -- I disagree with</p> <p>12 Dr. Epstein.</p> <p>13 Q. And this letter comes from</p> <p>14 FDA, right?</p> <p>15 A. Written by Dr. Epstein,</p> <p>16 right?</p> <p>17 Q. Right. And --</p> <p>18 A. I'm sorry, no, it's written</p> <p>19 by -- it seems to be written by Steven</p> <p>20 Musser.</p> <p>21 Q. Right. It's written to</p> <p>22 Dr. Epstein.</p> <p>23 A. It's written to Dr. -- so I</p> <p>24 guess I'm disagreeing with Steven M.</p>	<p style="text-align: right;">Page 428</p> <p>1 Q. You don't recall that?</p> <p>2 A. No. If you can just point</p> <p>3 it out to me again.</p> <p>4 Q. Just so I'm clear, you</p> <p>5 disagree with the position of the FDA as</p> <p>6 indicated in the April 1st, 2014, paper</p> <p>7 on migration, right?</p> <p>8 A. I'm -- I'm disagreeing again</p> <p>9 with a Dr. Steven Musser, Ph.D., who is</p> <p>10 the deputy director for Scientific</p> <p>11 Operation Center For Food Safety and</p> <p>12 Applied Nutrition. That's who I'm</p> <p>13 disagreeing with.</p> <p>14 Q. So going back to the Health</p> <p>15 Canada which we've previously marked as</p> <p>16 Exhibit 11.</p> <p>17 Do you see starting at</p> <p>18 Pages 19 through 21, the study authors of</p> <p>19 the Health Canada assessment are</p> <p>20 analyzing the scientific evidence in the</p> <p>21 context of the Bradford Hill criteria?</p> <p>22 A. Is there a specific area</p> <p>23 you'd like me to read or?</p> <p>24 Q. No.</p>
<p style="text-align: right;">Page 427</p> <p>1 Musser, Ph.D., who I -- I don't even know</p> <p>2 what area of practice he's -- he's the</p> <p>3 director of operations for Center of Food</p> <p>4 Safety and Applied Nutrition.</p> <p>5 I -- I don't know if he</p> <p>6 knows more about the female genital tract</p> <p>7 than I do, but my -- my guess is probably</p> <p>8 not. And if he's calling it indisputable</p> <p>9 in the absence of any study showing that</p> <p>10 it happens, that by definition is just</p> <p>11 wrong.</p> <p>12 Q. Doctor, you would agree,</p> <p>13 would you not, that in the Health Canada,</p> <p>14 the study authors, as part of the</p> <p>15 Bradford Hill have concluded that there</p> <p>16 is a biologically plausible mechanism by</p> <p>17 which talcum powder products can migrate</p> <p>18 from the perineum to the ovaries?</p> <p>19 MS. CURRY: Object to the</p> <p>20 form.</p> <p>21 THE WITNESS: I'd have --</p> <p>22 I'd have to read through it again.</p> <p>23 Can you point it to me?</p> <p>24 BY MS. GARBER:</p>	<p style="text-align: right;">Page 429</p> <p>1 Do you -- do you see that</p> <p>2 that's what that portion of the document</p> <p>3 is doing? It's an analysis of the</p> <p>4 evidence in the context of the Bradford</p> <p>5 Hill criteria.</p> <p>6 Is that true?</p> <p>7 A. They are addressing</p> <p>8 translocation in this section. I -- I</p> <p>9 assume that's part of a larger...</p> <p>10 Q. Doctor, is -- is strength of</p> <p>11 the association a criteria of Bradford</p> <p>12 Hill?</p> <p>13 A. Yes.</p> <p>14 Q. And consistency is a</p> <p>15 criteria of Bradford Hill?</p> <p>16 A. Yes. Which makes me think</p> <p>17 I'm looking at a different page.</p> <p>18 I'm sorry, which page are</p> <p>19 you on?</p> <p>20 Q. 19 through 20.</p> <p>21 A. 19.</p> <p>22 Q. Specificity as an aspect</p> <p>23 of --</p> <p>24 A. Oh, down at the bottom. I'm</p>

Kevin Holcomb, M.D.

<p style="text-align: right;">Page 430</p> <p>1 sorry. I was looking someplace else. 2 If you can just give me some 3 idea when we turn the page, if you're 4 talking top or bottom, I can probably get 5 there faster. 6 Q. Doctor, Pages 19 through 21, 7 the authors of Health Canada are 8 analyzing the scientific evidence in the 9 context of the Bradford Hill aspects or 10 criteria, are they not? 11 A. Yes. 12 Q. Thank you. And if you turn 13 to Page 20 -- sorry, Page 21, under the 14 heading of "Biologic Plausibility." You 15 agree that that's one of the aspects of 16 Bradford Hill, right? 17 A. Yes. And the first line 18 they have is, "Particles of talc are 19 hypothesized to migrate into the pelvis." 20 And that's very different from the 21 statement of the other doctor who said 22 it's indisputable. 23 MS. GARBBER: Motion to 24 strike as nonresponsive.</p>	<p style="text-align: right;">Page 432</p> <p>1 "The presence of talc in the ovaries has 2 been documented," and they cite to the 3 Heller 1996 paper, correct? 4 A. True. 5 Q. And they go on to say, "This 6 evidence" -- "This evidence of retrograde 7 transport supports the biologic 8 plausibility of the association between 9 perineal talc application and ovarian 10 exposure; however, the specific 11 mechanisms in the cascade of molecular 12 events by which talc cause ovarian cancer 13 have not been identified." And then they 14 cite to Taher 2018. 15 Did I read that correctly? 16 A. You read it correctly, yes. 17 Q. And Doctor, the Saed 2019 18 paper does, in fact, provide the 19 molecular events by which talc can cause 20 ovarian cancer. Can we agree with that? 21 MS. CURRY: Object to the 22 form. 23 THE WITNESS: No. 24 BY MS. GARBBER:</p>
<p style="text-align: right;">Page 431</p> <p>1 BY MS. GARBBER: 2 Q. Doctor, did I ask you a 3 question? 4 A. No. 5 Q. Should I get my time back 6 that you just wasted? 7 A. It's a small amount of time. 8 MS. CURRY: Object to the 9 form. 10 BY MS. GARBBER: 11 Q. All day long it's not a 12 small amount of time, is it, Doctor? 13 So let me ask you this, 14 under the biologic plausibility section 15 of the Bradford Hill analysis as 16 conducted by Health Canada, the study 17 authors indicate that, "Particles of talc 18 are hypothesized to migrate into the 19 pelvis and ovarian tissue, causing 20 irritation and inflammation." 21 I read that correctly, 22 right? 23 A. Yes. 24 Q. The authors go on to say,</p>	<p style="text-align: right;">Page 433</p> <p>1 Q. Okay. You have read the 2 Saed 2019 paper now? 3 A. I have. 4 Q. Not at the time of your 5 report, but you have? 6 MS. CURRY: Object to the 7 form. 8 THE WITNESS: I have. 9 BY MS. GARBBER: 10 Q. Did it provide a molecular 11 basis by which talc can cause ovarian 12 cancer? 13 A. It proposed a theory without 14 proving it. So when you say provide, I'm 15 assuming you mean that it proposed a 16 theory and then showed that that -- that 17 molecular change actually transformed 18 cells and causes cancer. 19 Q. You used the word "prove." 20 So the study provided statistically 21 significant findings of an association in 22 support of the experiment hypothesis, 23 correct? 24 A. I disagree.</p>

109 (Pages 430 to 433)

Kevin Holcomb, M.D.

Page 434	Page 436
<p>1 MS. CURRY: Object to the 2 form. 3 THE WITNESS: I disagree. 4 If the hypothesis is to say that 5 inflammation was the cause of 6 ovarian cancer, and in your study 7 you prove something like CA-125 8 goes up, and you consider that 9 proof of your hypothesis, I'd have 10 to say that's not the case. 11 BY MS. GARBER: 12 Q. Doctor, was that the only 13 finding of the Saed 2019 paper? 14 A. I'd be happy to look at the 15 rest of it. 16 Q. Well, you seem to remember 17 the CA-125 that was a corollary finding, 18 wasn't it? 19 MS. CURRY: Object to the 20 form. 21 THE WITNESS: If you have 22 the paper, again, I'd be happy to 23 look at the others. 24 BY MS. GARBER:</p>	<p>1 of -- 2 A. I'd have to look at it 3 again. 4 Q. Okay. And we'll do that. 5 So you see at the end of the 6 Bradford Hill analysis and the Health 7 Canada assessment, the authors conclude 8 that the data are indicative of a causal 9 effect, right? 10 A. That's what they state, yes. 11 Q. And so the authors have 12 found that there is a biologically 13 plausible mechanism by which talc can 14 migrate and talc can induce inflammation, 15 correct? 16 MS. CURRY: Object to the 17 form. 18 THE WITNESS: The authors 19 believe that Heller's findings are 20 evidence of retrograde 21 translocation of talc. 22 And that is a big 23 assumption. And so I can 24 understand how they would put</p>
Page 435	Page 437
<p>1 Q. Can you think of any other 2 molecular findings that were reported? 3 A. I remember -- 4 Q. For instance ROS or NOS 5 increasing with talc application? 6 MS. CURRY: Object to the 7 form. 8 THE WITNESS: I remember -- 9 and again, if you have the paper 10 I'd rather look at it again. But 11 I remember him making a statement 12 that reactive oxygen species 13 actually went up in the presence 14 of talc when in fact they were 15 actually lower than the controls 16 except for one concentration. 17 And then with the next 18 concentration, it actually went 19 back down. And yet, he concluded 20 that reactive oxygen species was 21 actually going up. 22 BY MS. GARBER: 23 Q. What was the conclusion of 24 the study authors in that paper, by way</p>	<p>1 those things together. But 2 there's no proof in Heller's study 3 where the talc particles came 4 from. 5 And so they're saying this 6 evidence of retrograde transports 7 supports biologic plausibility. 8 They cite a study that doesn't 9 prove retrograde transport and 10 says that is what I'm using to 11 support what I believe is 12 biologically plausible. 13 So yes, these authors are 14 making a statement and then citing 15 to something that never examined 16 retrograde transport. 17 BY MS. GARBER: 18 Q. Doctor, you have not 19 reviewed the Zervomanolakis or the Kunz 20 paper with regard to genital tract 21 peristalsis, have you? 22 A. No. 23 Q. Are you aware that there is 24 retrograde genital tract peristalsis</p>

110 (Pages 434 to 437)

Kevin Holcomb, M.D.

Page 438	Page 440
<p>1 during the woman's cycle?</p> <p>2 MS. CURRY: Object to the</p> <p>3 form.</p> <p>4 THE WITNESS: Yes. Of</p> <p>5 course I am. Does that mean that</p> <p>6 talc is able to retrograde</p> <p>7 translocate? I'm not sure. This</p> <p>8 is what often happens. People</p> <p>9 cite studies that don't prove what</p> <p>10 the -- the point that they're</p> <p>11 trying to make.</p> <p>12 BY MS. GARBER:</p> <p>13 Q. Okay. There's been data</p> <p>14 that have shown that particulate in a</p> <p>15 woman's genital tract can travel</p> <p>16 retrograde from the vagina to the</p> <p>17 fallopian tubes and the ovaries, correct?</p> <p>18 You are aware of this data?</p> <p>19 A. If you put her -- if you put</p> <p>20 her in the lithotomy position and give</p> <p>21 her a little oxytocin and -- yes, under</p> <p>22 those very unnatural conditions, there's</p> <p>23 studies supporting that.</p> <p>24 What I'm saying is I don't</p>	<p>1 A. True. And I've explained</p> <p>2 exactly how they make that connection.</p> <p>3 Q. Thank you.</p> <p>4 Let's talk about</p> <p>5 inflammation. You are aware that there</p> <p>6 is study data and peer-reviewed studies</p> <p>7 that indicate a biologically plausible</p> <p>8 mechanism by which talc can induce</p> <p>9 inflammation, correct?</p> <p>10 A. Is there a specific --</p> <p>11 MS. CURRY: Object to the</p> <p>12 form.</p> <p>13 THE WITNESS: -- study you'd</p> <p>14 like to review?</p> <p>15 BY MS. GARBER:</p> <p>16 Q. No, I'm just asking you,</p> <p>17 have you seen peer-reviewed studies that</p> <p>18 indicate talc can induce inflammation?</p> <p>19 A. I have not seen studies that</p> <p>20 I've read that I've been convinced. If</p> <p>21 you have a specific study that you'd like</p> <p>22 to review, I'm happy to go over --</p> <p>23 Q. Have you seen the Ness data?</p> <p>24 Either '99 or 2000?</p>
Page 439	Page 441
<p>1 see a single study -- and maybe you can</p> <p>2 quote one for me -- where they dusted the</p> <p>3 perineum of women and shown that that</p> <p>4 talc gets to the ovaries.</p> <p>5 Q. Based on what we know about</p> <p>6 talc and its carcinogenicity that would</p> <p>7 be an unethical study to conduct at this</p> <p>8 point, wouldn't it?</p> <p>9 MS. CURRY: Object to the</p> <p>10 form.</p> <p>11 MR. MIZGALA: Object to the</p> <p>12 form.</p> <p>13 THE WITNESS: Not if -- I</p> <p>14 would say not for a woman who's</p> <p>15 currently using talc.</p> <p>16 BY MS. GARBER:</p> <p>17 Q. Doctor, you would agree with</p> <p>18 me, wouldn't you, that there are study</p> <p>19 authors, peer-reviewed study authors, and</p> <p>20 in addition Health Canada, who have</p> <p>21 concluded that there is a biologically</p> <p>22 plausible mechanism by which talc can</p> <p>23 migrate from the genitals to the ovaries,</p> <p>24 true?</p>	<p>1 A. I did -- it's on my reliance</p> <p>2 list. If we can pull it out I'd be glad</p> <p>3 to go through it again with you.</p> <p>4 Q. Did the Ness authors</p> <p>5 conclude that there was a biologically</p> <p>6 plausible mechanism by which talc can</p> <p>7 induce inflammation?</p> <p>8 A. Again, I'd be happy to read</p> <p>9 the paper if you have it.</p> <p>10 Q. You're not sure?</p> <p>11 MS. CURRY: Object to the</p> <p>12 form.</p> <p>13 THE WITNESS: Oh, I don't</p> <p>14 remember everything off my</p> <p>15 reliance list off the top of my</p> <p>16 head, no.</p> <p>17 BY MS. GARBER:</p> <p>18 Q. Doctor, is it your opinion</p> <p>19 that -- is it your opinion that there is</p> <p>20 not a biologically plausible mechanism to</p> <p>21 support talc can migrate from the</p> <p>22 genitals to the ovaries and tubes because</p> <p>23 of the tubal ligation data?</p> <p>24 MS. CURRY: Object to the</p>

111 (Pages 438 to 441)

Kevin Holcomb, M.D.

<p style="text-align: right;">Page 442</p> <p>1 form.</p> <p>2 THE WITNESS: Please repeat</p> <p>3 that again.</p> <p>4 BY MS. GARBER:</p> <p>5 Q. Sure.</p> <p>6 Do you base your opinion</p> <p>7 that talcum powder products don't migrate</p> <p>8 to the ovaries based on tubal ligation</p> <p>9 and hysterectomy data?</p> <p>10 MS. CURRY: Object to the</p> <p>11 form.</p> <p>12 THE WITNESS: No. I base</p> <p>13 the fact that I don't have any</p> <p>14 proof of talc being able to</p> <p>15 migrate to the ovaries under</p> <p>16 normal situations. The tubal</p> <p>17 ligation data and the</p> <p>18 inconsistency of its protective</p> <p>19 impact makes me question even</p> <p>20 further.</p> <p>21 BY MS. GARBER:</p> <p>22 Q. Doctor, if you could pull</p> <p>23 out Taher 2018, Page 2. Do you see under</p> <p>24 the results there --</p>	<p style="text-align: right;">Page 444</p> <p>1 A. I'm assuming this is the</p> <p>2 results of the meta-analysis that hasn't</p> <p>3 been published?</p> <p>4 Q. Yes.</p> <p>5 A. Yes, that's what they say.</p> <p>6 Q. All right. And then a</p> <p>7 couple lines down it says, "This might be</p> <p>8 attributed to the fact that tubal</p> <p>9 ligation is usually performed at an</p> <p>10 earlier age, thus preventing entry of</p> <p>11 talc into the reproductive tract earlier</p> <p>12 and prolonged exposure to talc, compared</p> <p>13 to hysterectomy that is performed later</p> <p>14 in life where higher exposure has already</p> <p>15 taken place."</p> <p>16 It goes on to say, "In a</p> <p>17 recent meta-analysis," and then it cites</p> <p>18 70, "The authors reported a negative</p> <p>19 association with tubal ligation and</p> <p>20 hysterectomy with risk of ovarian</p> <p>21 cancer."</p> <p>22 Did I read that correctly?</p> <p>23 A. Yes, you've read everything</p> <p>24 very well so far.</p>
<p style="text-align: right;">Page 443</p> <p>1 A. I'm sorry -- Page 2.</p> <p>2 Q. -- that the study authors</p> <p>3 indicate that the most recent</p> <p>4 meta-analysis found a negative</p> <p>5 association with tubal ligation. That's</p> <p>6 what the authors say, right?</p> <p>7 A. This is an unpublished,</p> <p>8 un-peer-reviewed paper.</p> <p>9 Q. That's what the authors say</p> <p>10 in this paper, true?</p> <p>11 A. In this unpublished</p> <p>12 un-peer-reviewed paper, yes.</p> <p>13 Q. That's what the authors say,</p> <p>14 right?</p> <p>15 A. In this unpublished</p> <p>16 peer-reviewed paper, correct.</p> <p>17 Q. Turn to Page 33 please,</p> <p>18 Doctor. That the first full -- second</p> <p>19 full paragraph. It indicates, "Women</p> <p>20 with prior ligation of the fallopian</p> <p>21 tubes showed a significant reduction in</p> <p>22 risk," and then they cite a statistically</p> <p>23 significant odds ratio, right, against</p> <p>24 ovarian cancer?</p>	<p style="text-align: right;">Page 445</p> <p>1 Q. All right.</p> <p>2 A. It's that private schooling.</p> <p>3 Q. And -- and the authors go on</p> <p>4 to say as to the study that the authors</p> <p>5 there stated a highly plausible mechanism</p> <p>6 for the association --</p> <p>7 A. I'm sorry -- yes. As</p> <p>8 suggested by the author. Suggested.</p> <p>9 Q. Right. "Involving the</p> <p>10 blocking of ascent of such agents such as</p> <p>11 talc to the ovaries."</p> <p>12 Again, you disagree with</p> <p>13 these study -- with these two study</p> <p>14 authors that indicate that talc can</p> <p>15 ascend the female genital tract, right?</p> <p>16 A. It is a suggestion by the</p> <p>17 authors. It's not a proven point. These</p> <p>18 are conjecture and theory by those</p> <p>19 authors. And, yes, I would say</p> <p>20 apparently my bar is a little bit higher.</p> <p>21 I would like to see a study where you</p> <p>22 actually put talc on the perineum the way</p> <p>23 people put talc on the perineum and show</p> <p>24 that it gets to the ovaries. So, yes.</p>

Kevin Holcomb, M.D.

<p style="text-align: right;">Page 446</p> <p>1 And -- and I find, outside 2 of this unpublished meta-analysis, when 3 you get to the individual studies it 4 becomes much less consistent on this 5 protective impact of tubal ligation with 6 regard to talc. 7 MS. GARBER: Objection. 8 Motion to strike as nonresponsive. 9 BY MS. GARBER: 10 Q. Doctor, if you could turn 11 back to Health Canada and Page 18. And 12 I'll just point to where I'm reading, 13 Doctor. Right here. 14 Do you see where I am? 15 Doctor, it reads: "There is 16 support for an association of 17 inflammation and increased risk of 18 ovarian cancer." And it cites to the 19 National Academy of Sciences, Engineering 20 and Medicine in 2016 in the Rasmussen 21 paper. 22 Doctor, that's what these 23 study authors who did an analysis -- 24 A. Can -- can -- I'm sorry,</p>	<p style="text-align: right;">Page 448</p> <p>1 fact that the NSAID data do not support 2 reduction of risk of ovarian cancer? 3 MS. CURRY: Object to the 4 form. 5 THE WITNESS: The main 6 reason why I hold that opinion is 7 because I have seen no evidence of 8 chronic inflammation in the 9 genital tract from perineal use of 10 talc. 11 In the Heller study, in the 12 case that they looked for evidence 13 of clinical information, and -- 14 and we know what it looks like 15 with talc, because there's years 16 of using it in pleurodesis, it 17 causes granulomas. 18 I -- we -- we present every 19 STIC lesion, a serous tubular 20 intraepithelial carcinoma at 21 Cornell. We present it as part of 22 our tumor board. And so I've seen 23 a lot of STIC lesions. I've seen 24 a lot of p53 signatures.</p>
<p style="text-align: right;">Page 447</p> <p>1 I'll let you finish. 2 Q. -- concluded about the mode 3 of action, correct? 4 MS. CURRY: Object to the 5 form. 6 THE WITNESS: Yes, and 7 interestingly, I -- I would be 8 glad to look at the Rasmussen 9 paper. I believe it was actually 10 a paper that was negative, that 11 there was a paper that didn't show 12 a reduce in the risk of ovarian 13 cancer with -- with 14 antiinflammatories. 15 BY MS. GARBER: 16 Q. And, Doctor, I'm glad you 17 mentioned antiinflammatories. Because is 18 the other basis for your opinion that 19 talc, while it increases inflammation, 20 doesn't cause ovarian -- talcum powder -- 21 strike that. 22 Another basis for your 23 opinion that talcum powder products do 24 not cause ovarian cancer based on the</p>	<p style="text-align: right;">Page 449</p> <p>1 I've not ever seen a case 2 with a granuloma or any evidence 3 of granulomatous inflammation or 4 any other sort of inflammation, 5 and so that's the real -- the -- 6 the other thing that you're 7 mentioning, the inconsistency of 8 whether antiinflammatories reduce 9 the risk of ovarian cancer just 10 further confirms my -- my belief. 11 But it's really the fact 12 that I've seen the precursor 13 lesion for high grade serous 14 carcinoma, and I've never seen it 15 in conjunction with any evidence 16 of granulomatous inflammation. 17 BY MS. GARBER: 18 Q. Okay. Let's take both of 19 those, because I think you mentioned two 20 different things there. 21 As to what you see when you 22 look at the tissue pathology, -- that's 23 what you're referencing, right, what 24 you're seeing microscopically in the path</p>

Kevin Holcomb, M.D.

Page 450	Page 452
<p>1 slides?</p> <p>2 A. Yes.</p> <p>3 Q. And --</p> <p>4 A. I would argue in -- in</p> <p>5 ovarian cancer cases as well, I don't see</p> <p>6 granulomas.</p> <p>7 Q. You mean macroscopically</p> <p>8 when you're doing surgery?</p> <p>9 A. No, I mean microscopically.</p> <p>10 I also scrub out and look at all my</p> <p>11 frozen sections. And we present every</p> <p>12 new patient in a multi-disciplinary tumor</p> <p>13 board where we look at the slides. So</p> <p>14 there's not an ovarian cancer patient</p> <p>15 that I take care of that I haven't seen</p> <p>16 her histologic slides.</p> <p>17 Q. Have you seen testimony</p> <p>18 where there is -- strike that.</p> <p>19 Have you seen data that</p> <p>20 would suggest that you're not seeing</p> <p>21 evidence of acute inflammation because</p> <p>22 the talc and its effects have been</p> <p>23 subsumed by tumor? In other words,</p> <p>24 that's a snapshot in time when there's</p>	<p>1 at the time of precancer, I've not</p> <p>2 seen it. And if it's not there in</p> <p>3 the precancerous phase, when was</p> <p>4 it there?</p> <p>5 BY MS. GARBER:</p> <p>6 Q. Is it your opinion that all</p> <p>7 epithelial ovarian cancers begin in the</p> <p>8 fallopian tube?</p> <p>9 A. No.</p> <p>10 Q. Okay. Let's talk about the</p> <p>11 NSAIDs, the NSAID data.</p> <p>12 You've looked at some</p> <p>13 studies about NSAIDs and their effect</p> <p>14 upon the risk of --</p> <p>15 A. Yes.</p> <p>16 Q. -- ovarian cancer right?</p> <p>17 A. Yes, I have.</p> <p>18 Q. Would you agree with me that</p> <p>19 the aspirin data seem to indicate a</p> <p>20 decreased risk in ovarian cancer?</p> <p>21 MS. CURRY: Object to the</p> <p>22 form.</p> <p>23 THE WITNESS: I'm not sure</p> <p>24 if that's consistent in every --</p>
Page 451	Page 453
<p>1 carcinogenic transformation, and what</p> <p>2 you're seeing over here years later</p> <p>3 you're not going to see the evidence of</p> <p>4 the chronic inflammation, correct?</p> <p>5 MS. CURRY: Object to the</p> <p>6 form.</p> <p>7 THE WITNESS: Maybe you</p> <p>8 misunderstood my description of</p> <p>9 what we do. I said look at every</p> <p>10 invasive cancer and we present</p> <p>11 every STIC.</p> <p>12 And so that's precancer.</p> <p>13 That is a precursor to high grade</p> <p>14 serous ovarian cancer. And now we</p> <p>15 believe there's a p53 signature</p> <p>16 that's even earlier. And I will</p> <p>17 tell you that I've never seen any</p> <p>18 evidence of inflammation in any of</p> <p>19 those lesions, nor have I read of</p> <p>20 anybody showing granulomatous</p> <p>21 inflammation in any of those</p> <p>22 lesions.</p> <p>23 So you may believe it</p> <p>24 disappears later. I'm saying even</p>	<p>1 in every study. I just want to</p> <p>2 get to my report in that area, if</p> <p>3 that's okay.</p> <p>4 BY MS. GARBER:</p> <p>5 Q. Okay. Doctor, shall we go</p> <p>6 off the record?</p> <p>7 A. You can. It's not going to</p> <p>8 take me long.</p> <p>9 THE VIDEOGRAPHER: The time</p> <p>10 is 5:49. Going off the record.</p> <p>11 (Brief pause.)</p> <p>12 THE VIDEOGRAPHER: The time</p> <p>13 is 5:49 p.m. Back on the record.</p> <p>14 THE WITNESS: So Bonovas, et</p> <p>15 al., is a meta-analysis that</p> <p>16 showed antiinflammatory drug use</p> <p>17 did not reduce ovarian cancer.</p> <p>18 Ni, et al., did a pooled</p> <p>19 analysis of 13 case-control</p> <p>20 studies, one clinical trial, three</p> <p>21 cohort studies. Also found no</p> <p>22 efforts of an association between</p> <p>23 aspirin use and ovarian cancer and</p> <p>24 did not find strong evidence of an</p>

114 (Pages 450 to 453)

Kevin Holcomb, M.D.

Page 454	Page 456
<p>1 association between non-aspirin 2 NSAID use and ovarian cancer. 3 BY MS. GARBER: 4 Q. Doctor, did I have a 5 question pending? 6 A. You had asked me -- yeah. 7 You did. That's why we went off. 8 Remember I was looking for the -- 9 Q. Okay. Have you seen the -- 10 I don't know how to pronounce it -- 11 Q-I-A-O, 2018, study with regard to -- 12 with regard to aspirin and its effects on 13 ovarian cancer? 14 A. I have not. 15 Q. Have you seen Trabert 2013 16 study wherein the study authors found 17 that use of antiinflammatory aspirin was 18 associated with a reduction of risk of 19 ovarian cancer? 20 A. I believe that -- 21 MS. CURRY: Object to the 22 form. 23 THE WITNESS: I believe 24 that's in my -- my report that's</p>	<p>1 cancer to take an NSAID, Tylenol -- well, 2 Tylenol really hasn't shown much 3 difference. But even aspirin. 4 That's different from a 5 woman who has -- or a man who has 6 familial adenomatous polyposis. There's 7 certain situations where the data is so 8 strong that you can prevent cancer, it's 9 actually recommended to use aspirin to 10 prevent it. And we don't do that in GYN 11 oncology. 12 And so I'd have to ask you, 13 not only do I not believe this, but why 14 is the GYN oncology not recommending 15 NSAID and aspirin use if it is so proven 16 that it decreases ovarian cancer risk? 17 It would be -- 18 MS. GARBER: Objection. 19 Objection. Motion to strike as 20 nonresponsive. 21 BY MS. GARBER: 22 Q. Doctor, you're talking in 23 paragraphs, and you're not answering my 24 question. I'm going to just ask you to</p>
Page 455	Page 457
<p>1 saying -- to show the 2 inconsistencies. I gave you two 3 examples of studies, one including 4 meta-analysis, and showing no 5 reduced ovarian cancer, and the 6 studies that you mentioned that 7 show that there was a reduction. 8 BY MS. GARBER: 9 Q. Do you agree, Doctor, that 10 there are data on both sides for both 11 aspirin and nonsteroidal 12 antiinflammatories that go both ways? In 13 other words, there's some data that show 14 a decreased risk of ovarian cancer and 15 some data that do not for both aspirin 16 and NSAIDs? 17 A. I do believe that if there 18 was powerful enough data to support the 19 use of antiinflammatories to prevent the 20 deadliest GYN malignancy, this would be a 21 common recommendation for patients to 22 use. We don't tell BRCA mutation 23 patients to take NSAIDs. We don't tell 24 the women at the highest risk of ovarian</p>	<p>1 indulge me, please. 2 MS. CURRY: I disagree. 3 BY MS. GARBER: 4 Q. My question -- 5 MS. CURRY: That was 6 directly responsive to the 7 question. 8 BY MS. GARBER: 9 Q. My question was, do you 10 agree that there are data for aspirin and 11 NSAIDs that go both ways, they decrease 12 the risk, and other studies do not show 13 that? 14 A. The reason why for speaking 15 in paragraphs -- 16 Q. I didn't ask you why. 17 A. -- is because it's still 18 clearly stated in my report -- 19 Q. Doctor, I didn't ask you why 20 you're speaking in paragraphs. 21 A. But it says so in my report. 22 And I gave you the examples. And we just 23 went through them one by one. I gave you 24 two examples where it did, and two</p>

115 (Pages 454 to 457)

Kevin Holcomb, M.D.

Page 458	Page 460
<p>1 examples it didn't. And then you follow 2 up a question -- 3 Q. If you're not -- if you're 4 not going to answer my question -- 5 A. Because -- 6 Q. -- I think we're going to 7 have to call the Court because we're 8 nearly done, and you're talking in 9 paragraphs and you're not responding to 10 my question. 11 A. But you're asking -- 12 MS. SHARKO: The order 13 doesn't allow you to criticize his 14 answer. So please stop. 15 THE WITNESS: You're asking 16 questions that -- 17 MS. O'DELL: That's not 18 true, Susan. Completely not true. 19 THE WITNESS: -- have clear 20 evidence. You're saying have I -- 21 I cited in my report data that 22 went both ways. And then you turn 23 around and ask me, do you believe 24 that data goes both ways? And I</p>	<p>1 cancer. 2 Do you recall that data? 3 MS. CURRY: Object to the 4 form. 5 THE WITNESS: Yes. 6 BY MS. GARBER: 7 Q. Why did you cite those data? 8 A. Couple reasons. 9 Penninkilampi, in trying to explain the 10 way exactly what were you trying to 11 explain, he's saying that I know it's 12 inconsistent, the data on nonsteroidals. 13 He's saying, I know it doesn't look in 14 support of my argument for my biologic 15 plausibility. 16 But maybe -- maybe NSAIDs 17 don't work because they don't -- they 18 only -- they prevent -- they work on COX. 19 And COX expression is low in these cells 20 anyway. And that's why you don't see a 21 more impressive -- so he's explaining why 22 this data that you're saying is -- is as 23 unimpressive as it is. 24 And so I read in</p>
Page 459	Page 461
<p>1 cited. 2 BY MS. GARBER: 3 Q. I never said in your report. 4 Do you agree that there are 5 peer-reviewed published studies on the 6 topic of anti-inflammatories, aspirin and 7 NSAIDs -- NSAIDs, that go both ways, some 8 data show a decreased risk and other data 9 do not? 10 MS. CURRY: Object to the 11 form. 12 BY MS. GARBER: 13 Q. Do you agree? 14 A. I do agree. And that's the 15 reason -- the fact that it's gone both 16 ways is the reason why we do not 17 recommend nonsteroidal use or aspirin use 18 to prevent it. 19 Q. And Doctor, you don't 20 know -- strike that. 21 You cited on your 22 supplemental report some data that were 23 cited in the Penninkilampi paper about 24 the COX expression in epithelial ovarian</p>	<p>1 Dr. Saenz -- her deposition, she 2 mentioned some basic science research by 3 Dr. Dineo Khabele, who I happened to have 4 been a resident with back at Cornell 5 years ago. 6 And so that piqued my 7 interest. And I was curious to see what 8 is she doing in her lab, and so I 9 actually went back and I looked at the 10 studies that she was showing to see that 11 Penninkilampi actually had misstated the 12 fact that Type 2 tumors, high grade 13 serous carcinomas, actually expressed 14 COX-1. And Type 1 expressed COX-2. 15 So this idea that inhibitors 16 of COX, that NSAIDs, that they don't 17 work, or aspirin doesn't work because 18 there's low expression of this thing in 19 the first place, that doesn't make sense. 20 If -- if -- you'd have to explain 21 something else. 22 Maybe it doesn't make a 23 difference because ovarian cancer is not 24 caused by inflammation.</p>

116 (Pages 458 to 461)

Kevin Holcomb, M.D.

<p style="text-align: right;">Page 462</p> <p>1 Q. You didn't read the Wilson 2 2015 paper with regard to COX -- COX 3 expression in epithelial ovarian tissue, 4 did you? 5 MS. CURRY: Object to the 6 form. 7 THE WITNESS: Whose -- whose 8 paper? I'm sorry. 9 BY MS. GARBER: 10 Q. Wilson, et al.? 11 A. If you can show it to me I'd 12 let you know. I don't think so. 13 MS. O'DELL: Counsel, please 14 don't show something to the 15 witness. 16 MS. CURRY: I'm just -- 17 you're referring to -- you just 18 said Wilson 2000 -- 19 MS. O'DELL: Let me finish. 20 That's the third time -- 21 MS. CURRY: Hang on a minute 22 and let me explain. It's not the 23 third time. 24 MS. O'DELL: It's the third</p>	<p style="text-align: right;">Page 464</p> <p>1 That's the only thing I was 2 doing. That is not inappropriate. 3 MS. O'DELL: It is 4 inappropriate -- 5 MS. CURRY: I disagree. 6 MS. O'DELL: -- and the 7 three instances that I've referred 8 to are not occasions when the Elmo 9 was in use, so -- 10 MS. CURRY: Well, I think 11 you are mischaracterizing what has 12 happened today. 13 MS. O'DELL: That is not 14 true. 15 BY MS. GARBER: 16 Q. Doctor, is the basis for 17 your opinion that talc does not induce 18 inflammation which leads to ovarian 19 cancer based on pleurodesis data? 20 MS. CURRY: Object to the 21 form. 22 THE WITNESS: No. 23 BY MS. GARBER: 24 Q. Pleurodesis does -- talc</p>
<p style="text-align: right;">Page 463</p> <p>1 time I've seen you do it and I 2 haven't said anything. But that's 3 not appropriate -- 4 MS. GARBER: I've seen you 5 do it as well. 6 MS. CURRY: Excuse me. 7 Excuse me. I've pointed out where 8 you were trying to show something 9 on the Elmo, and he's trying to 10 find it, where it is on the 11 document to help speed things 12 along. 13 MS. O'DELL: Those -- 14 MS. CURRY: What I just 15 referred to him -- excuse me. Let 16 me finish speaking, please. 17 What I just pointed out was, 18 when you say Wilson 2015, it's -- 19 you're not giving any further 20 information about the article. 21 So I'm pointing out that 22 it's the one on his supplemental 23 list of items considered that 24 we've produced to you today.</p>	<p style="text-align: right;">Page 465</p> <p>1 pleurodesis has been shown to increase 2 inflammation in pleural tissue, correct? 3 A. But not cancer. Yes, it 4 increases -- 5 Q. That wasn't my question. 6 A. It increases inflammation. 7 Does not cause cancer. 8 So the reason why I don't 9 think inflammation -- 10 Q. Doctor, I didn't ask you the 11 reason. Did I? 12 A. Oh, I'm sorry. I thought I 13 was here to clarify my positions. I'll 14 wait for the questions. 15 Q. Thank you. I really 16 appreciate that. You've got to let me 17 get there. 18 A. You don't get there. 19 Q. I will if you don't stop 20 talking in paragraphs. 21 Doctor, did you read the 22 Ghio 2007 study with regard to 23 pleurodesis, talc pleurodesis? 24 A. Can you produce it for me so</p>

Kevin Holcomb, M.D.

Page 466	Page 468
<p>1 I can let you know? 2 Q. I will. 3 While she's pulling that, 4 I'll ask you this. You indicate that 5 talc pleurodesis does not induce cancer, 6 is that fair, what you said? 7 A. Yes. 8 Q. And the number one 9 indication for talc pleurodesis is 10 malignant pleural effusions, right? 11 A. Yes. 12 Q. And so those patients 13 already have cancer and are likely end 14 stage, right? 15 A. It had been used for years 16 on patients without malignancy. The 17 reason why it's used on patients -- 18 Q. Did you say yes? 19 A. Say this again? 20 Q. Did you say yes to my -- to 21 my question? 22 MS. CURRY: Objection. 23 Please don't interrupt him -- 24 BY MS. GARBER:</p>	<p>1 Pleural Effusions." 2 (Document marked for 3 identification as Exhibit 4 Holcomb-26.) 5 BY MS. GARBER: 6 Q. Nonmalignant pleural 7 effusions are what for the lay listener? 8 MS. CURRY: Object to the 9 form. 10 MS. SHARKO: What exhibit is 11 this now? 12 MS. BROWN: 26. 13 MS. SHARKO: Pardon me? 14 MS. BROWN: 26. 15 BY MS. GARBER: 16 Q. What's a nonmalignant 17 pleural effusion? 18 A. A nonmalignant pleural 19 effusion is one where you have fluid 20 surrounding the lung but it's not from a 21 cancer. 22 Q. All right. And -- and this 23 paper is authored by Andrew Ghio and 24 Victor Roggli.</p>
Page 467	Page 469
<p>1 Q. Did you say yes to my 2 question? I didn't ask you for the 3 reason. 4 A. Your -- your question is? 5 Q. Did you say yes? 6 A. Can you ask the question 7 again? I want to -- just repeat it. 8 Q. I said: "And those patients 9 have cancer and are likely end stage, 10 right?" 11 And you said: "It has been 12 used for years on patients without 13 malignancy. The reason --" 14 And then I said: "Did you 15 say yes?" 16 You said? 17 A. Yes. In those patients that 18 have malignancy, they are likely end 19 stage. As opposed to the patients who 20 don't have malignancy for years that has 21 been used. 22 Q. Doctor, the title of this 23 study is "Talc Should Not Be Used For 24 Pleurodesis in Patients With Nonmalignant</p>	<p>1 Do you see that? 2 MS. CURRY: Object to the 3 form. 4 THE WITNESS: Yes. 5 BY MS. GARBER: 6 Q. Okay. In the first 7 paragraph, it begins, however, it says, 8 "However, there should continue to be 9 concern regarding use of talc for 10 pleurodesis in individuals with 11 nonmalignant pleural effusions and 12 spontaneous pneumothorax. This dilemma 13 results from a possible increased risk of 14 malignant mesothelioma in those patients 15 treated with talc. Consequently, an 16 alternative agent should be employed in 17 any individual without malignancy 18 requiring pleurodesis." 19 Did I read that correctly? 20 A. You read that correctly 21 again. 22 THE VIDEOGRAPHER: Can 23 you -- your hair is on top of the 24 mic.</p>

118 (Pages 466 to 469)

Kevin Holcomb, M.D.

Page 470	Page 472
<p>1 MS. GARBER: Sorry.</p> <p>2 THE VIDEOGRAPHER: Thanks.</p> <p>3 BY MS. GARBER:</p> <p>4 Q. Doctor, do you think that --</p> <p>5 that peer-reviewed published data</p> <p>6 indicate that there is a dose-response</p> <p>7 with regard to talc and risk of ovarian</p> <p>8 cancer?</p> <p>9 A. I believe that that's one of</p> <p>10 the weaknesses is it's not consistently</p> <p>11 shown.</p> <p>12 Q. But you do agree that there</p> <p>13 are peer-reviewed studies which show a</p> <p>14 dose-response, correct?</p> <p>15 MS. CURRY: Object to the</p> <p>16 form.</p> <p>17 THE WITNESS: I've seen</p> <p>18 studies that are peer reviewed and</p> <p>19 published that have only two</p> <p>20 levels of exposure, and one is</p> <p>21 higher than the other and they</p> <p>22 call that a dose-response.</p> <p>23 So what I've seen in the</p> <p>24 literature, people define</p>	<p>1 A. Yeah. I mean, I can't --</p> <p>2 I'm going to have to watch up here</p> <p>3 because it's too small.</p> <p>4 Q. Are you there --</p> <p>5 A. Yeah, I'm going to have to</p> <p>6 sit it here because --</p> <p>7 Q. -- in your version?</p> <p>8 MS. CURRY: Can I show him</p> <p>9 my version which is --</p> <p>10 THE WITNESS: I mean</p> <p>11 literally, it's this. That's</p> <p>12 Table 3. You want me to read that</p> <p>13 and give you an opinion?</p> <p>14 MS. GARBER: Let me see</p> <p>15 yours, Ms. Curry, if you could.</p> <p>16 Yes, please show that to</p> <p>17 him. Thank you.</p> <p>18 BY MS. GARBER:</p> <p>19 Q. Doctor, in the Berge study</p> <p>20 it indicates that with the duration of</p> <p>21 talc use greater than ten years, defined</p> <p>22 as ten years, there is a statistically</p> <p>23 significant relative risk, correct?</p> <p>24 A. I'm just trying to make sure</p>
Page 471	Page 473
<p>1 dose-response in a lot of</p> <p>2 different ways. So I'd have to</p> <p>3 agree with you, yes.</p> <p>4 Penninkilampi does that.</p> <p>5 Two dose levels and says there's a</p> <p>6 dose-response.</p> <p>7 (Document marked for</p> <p>8 identification as Exhibit</p> <p>9 Holcomb-27.)</p> <p>10 BY MS. GARBER:</p> <p>11 Q. I'm going to mark as</p> <p>12 Exhibit 27 the Berge paper that you've</p> <p>13 referenced many times today, Doctor.</p> <p>14 And, Doctor, if you can turn</p> <p>15 to -- if you can turn to -- well, in this</p> <p>16 paper, unfortunately there isn't page</p> <p>17 numbers.</p> <p>18 And so this table is Table</p> <p>19 3, and it appears about five, six pages</p> <p>20 forward from the end of the document.</p> <p>21 Table 3.</p> <p>22 A. Sure.</p> <p>23 Q. If you want, we can look at</p> <p>24 it here. Do you see Table 3, Doctor?</p>	<p>1 I understand what they're looking at</p> <p>2 here.</p> <p>3 Q. That's what the table says,</p> <p>4 right?</p> <p>5 A. Give me one second, ma'am.</p> <p>6 I'll be right with you.</p> <p>7 MS. GARBER: Let's go off</p> <p>8 the record then.</p> <p>9 THE VIDEOGRAPHER: All</p> <p>10 right. The time is 6:03 p.m. Off</p> <p>11 the record.</p> <p>12 (Brief pause.)</p> <p>13 MS. SHARKO: For the record,</p> <p>14 we object to this. I don't think</p> <p>15 it's appropriate. I don't think</p> <p>16 it's appropriate, but it's late in</p> <p>17 the day, and I assume that the</p> <p>18 plaintiffs are almost done in any</p> <p>19 event.</p> <p>20 MS. GARBER: You're correct</p> <p>21 in that regard.</p> <p>22 THE VIDEOGRAPHER: We are</p> <p>23 back on the record. The time is</p> <p>24 6:04 p.m.</p>

119 (Pages 470 to 473)

Kevin Holcomb, M.D.

<p style="text-align: right;">Page 474</p> <p>1 BY MS. GARBER: 2 Q. Doctor, these data here that 3 are presented in Table 3, they show 4 duration and frequency of talc use, 5 right? 6 A. Yes. 7 Q. In the meta-analysis? 8 A. Yes. 9 Q. Correct? 10 And for the duration defined 11 as ten years, the relative risk is 12 statistically significant at 1.16, right? 13 A. The only thing I'm not -- I 14 have to say I'm not sure what's going on 15 here, and I didn't want to hold up more 16 time. Are they saying if you compare 17 studies in this 12-risk estimate and look 18 at someone who had less than ten years 19 use and more than ten years use, and then 20 say the relative risk between those two 21 is 1.16, and a confidence interval that 22 comes close but doesn't cross one, then 23 you're -- if it's a -- if it's just 24 splitting it in two, and say well ten is</p>	<p style="text-align: right;">Page 476</p> <p>1 THE WITNESS: Yes. But not 2 together. They're saying duration 3 in one and frequency in the other. 4 So they're saying that -- but I 5 think they've just split this in 6 two. 7 BY MS. GARBER: 8 Q. And, Doctor, if you go back 9 to the abstract, first page of this 10 study. 11 A. Right. 12 Q. Okay. Second-to-last 13 sentence. It says, "This meta-analysis 14 resulted in a weak but statistically 15 significant association between genital 16 use of talc and ovarian cancer, which 17 appears to be limited to serous carcinoma 18 with a suggestion of a dose-response." 19 Do you see that? 20 A. Yeah. 21 Q. Those were the authors' 22 words, right, suggestion of a 23 dose-response? 24 A. Suggestion, yes.</p>
<p style="text-align: right;">Page 475</p> <p>1 the split-off and I'm going to look at 2 less than ten and more than ten, that's 3 not a dose-response. You can't make a 4 dose-response on just two observations. 5 And I think that may be what 6 they're doing on the second one as well. 7 But to be perfectly honest, I'm not sure. 8 I'd have to look at the methods to figure 9 out what they're doing here. But it 10 seems like a -- like a -- basically 11 just -- what's the term I'm looking for? 12 Just two options, less than ten years, 13 more than ten years. 14 Q. Doctor, let me ask you this. 15 Does Table 3 -- 16 A. I guess I don't understand 17 exactly what they did here. 18 Q. Yeah. Okay. That's fair. 19 Does Table 3 present 20 duration and frequency of talc use that 21 present statistically significant 22 results? 23 MS. CURRY: Object to the 24 form.</p>	<p style="text-align: right;">Page 477</p> <p>1 Q. Okay. And then -- 2 A. And I think they're using 3 suggestion because they just did a 4 dichotomous -- that's the word that I was 5 looking for, dichotomous -- a dichotomous 6 evaluation with just -- and you can't 7 prove a dose-response. Because if they 8 were doing a test for dose-response, they 9 met statistical significance. And you 10 know how much I like confidence 11 intervals. They would say that they 12 found a dose-response. But they're 13 saying it's a suggestion of a 14 dose-response because they didn't do that 15 sort of analysis. 16 Q. Doctor, Health Canada 17 concluded there was a dose-response in 18 their Bradford Hill, right, under their 19 biologic gradient assessment? 20 MS. CURRY: Object to the 21 form. 22 THE WITNESS: I'd have to 23 look -- have to look back at that. 24 BY MS. GARBER:</p>

120 (Pages 474 to 477)

Kevin Holcomb, M.D.

Page 478	Page 480
<p>1 Q. You don't remember?</p> <p>2 A. No, I don't.</p> <p>3 Q. All right.</p> <p>4 A. Can you tell me which page</p> <p>5 you are talking about?</p> <p>6 Q. Can I ask you a few more</p> <p>7 questions?</p> <p>8 Were you provided by</p> <p>9 Johnson & Johnson counsel any testing of</p> <p>10 talcum powder products by Dr. Longo with</p> <p>11 regard to historical samples of talcum</p> <p>12 powder products?</p> <p>13 A. No.</p> <p>14 Q. Were you provided by Johnson</p> <p>15 & Johnson with any internal Johnson &</p> <p>16 Johnson company testing of their talcum</p> <p>17 powder products for asbestos or fibrous</p> <p>18 talc?</p> <p>19 A. No.</p> <p>20 Q. Were you provided with any</p> <p>21 company witness testimony with regard to</p> <p>22 testing of talcum powder products?</p> <p>23 A. I hadn't requested any of</p> <p>24 these, and no, I wasn't provided.</p>	<p>1 said all that to her, she said, "I just</p> <p>2 need to know, Doctor, should I use it?</p> <p>3 Is it safe? Yes or no?" what would your</p> <p>4 response be?</p> <p>5 MS. CURRY: Object to the</p> <p>6 form.</p> <p>7 THE WITNESS: I'd want to</p> <p>8 ask her why she uses it. I'm</p> <p>9 going to make another assumption.</p> <p>10 The fact that she's asking me</p> <p>11 again after that explanation is</p> <p>12 that she's concerned. And I would</p> <p>13 say, if you're concerned maybe you</p> <p>14 should find an alternative product</p> <p>15 because you're concerned, not</p> <p>16 because I think it causes ovarian</p> <p>17 cancer. But I don't see why you</p> <p>18 would stress yourself out over</p> <p>19 this.</p> <p>20 BY MS. GARBER:</p> <p>21 Q. And, Doctor, if your patient</p> <p>22 said, "I just need to know, is using</p> <p>23 Johnson & Johnson talcum powder products</p> <p>24 that contain asbestos, is that safe for</p>
Page 479	Page 481
<p>1 Q. So, Doctor, let me ask you</p> <p>2 this. I want you to assume that talcum</p> <p>3 powder products contain asbestos, and a</p> <p>4 patient of yours has asked you, is it</p> <p>5 safe to use talcum powder products on my</p> <p>6 genitals. What would be your response?</p> <p>7 A. Well, my first step would be</p> <p>8 to disclose that I'm involved in this</p> <p>9 litigation.</p> <p>10 And then I would tell her,</p> <p>11 pretty much what I would say without that</p> <p>12 assumption, that there are some, in my</p> <p>13 opinion, weaker designed studies showing</p> <p>14 a weak, as other people agree, increased</p> <p>15 risk of ovarian cancer. And other</p> <p>16 weaker -- other weakly designed studies</p> <p>17 that show no difference, and it seems to</p> <p>18 be about a 50/50 thing, and then cohort</p> <p>19 studies that show no increased risk.</p> <p>20 And I would tell the patient</p> <p>21 overall there's not sufficient evidence</p> <p>22 to suggest that talcum powder causes</p> <p>23 ovarian cancer.</p> <p>24 Q. And, Doctor, if after you</p>	<p>1 me to use? Yes or no?"</p> <p>2 MS. CURRY: Object to the</p> <p>3 form.</p> <p>4 THE WITNESS: And this is</p> <p>5 with my assumption that there's</p> <p>6 asbestos in the product?</p> <p>7 BY MS. GARBER:</p> <p>8 Q. Right.</p> <p>9 A. And I'm going to make</p> <p>10 another assumption that there were</p> <p>11 asbestos in the products that was studied</p> <p>12 in this totality of the evidence that I</p> <p>13 reviewed. And I would -- I'm not going</p> <p>14 to repeat it for the sake of time, but I</p> <p>15 would have the same exact discussion with</p> <p>16 her.</p> <p>17 Q. You would say that it's safe</p> <p>18 to use?</p> <p>19 A. I would say that, given your</p> <p>20 assumption, there's asbestos in this</p> <p>21 talcum powder. The totality of the data</p> <p>22 using the same product that you say has</p> <p>23 asbestos in it, does not convince me that</p> <p>24 it causes ovarian cancer. So I would --</p>

121 (Pages 478 to 481)

Kevin Holcomb, M.D.

Page 482	Page 484
<p>1 that's what I would say to her.</p> <p>2 Q. Would you say that it was</p> <p>3 then safe to use?</p> <p>4 A. Again, I'm telling you that</p> <p>5 there is no convincing evidence that this</p> <p>6 powder causes ovarian cancer. And that's</p> <p>7 where I would leave it.</p> <p>8 Q. Okay. Let me turn to</p> <p>9 another hypothetical.</p> <p>10 I want you to assume that</p> <p>11 Johnson & Johnson's talcum powder</p> <p>12 products are found to contain fibrous</p> <p>13 talc and your patient asks you the same</p> <p>14 question, is it safe for me to use</p> <p>15 Johnson & Johnson's talcum powder</p> <p>16 products that contain fibrous talc on my</p> <p>17 genitals, what would your response be?</p> <p>18 MS. CURRY: Object to the</p> <p>19 form.</p> <p>20 THE WITNESS: In this</p> <p>21 hypothetical situation, can I</p> <p>22 assume that that same Johnson &</p> <p>23 Johnson that has fibrous talc was</p> <p>24 the same stuff used in all the</p>	<p>1 you, is it safe to apply this product to</p> <p>2 my genitals.</p> <p>3 A. Okay. I'm going to assume</p> <p>4 then that the product that you're</p> <p>5 describing is the same product that was</p> <p>6 used in the totality of the data that I</p> <p>7 reviewed. And I would tell her the exact</p> <p>8 same story, that there's some weaker</p> <p>9 studies suggesting a modest or weak</p> <p>10 inconsistent positive association, and</p> <p>11 stronger studies showing no association.</p> <p>12 And in its totality, I would say there's</p> <p>13 no compelling evidence that that product</p> <p>14 that you're describing increases her risk</p> <p>15 for ovarian cancer.</p> <p>16 Q. Do you go to those data</p> <p>17 because you assume there's asbestos in</p> <p>18 Johnson & Johnson's products always?</p> <p>19 MS. CURRY: Object to the</p> <p>20 form.</p> <p>21 THE WITNESS: Do I go to</p> <p>22 what data?</p> <p>23 BY MS. GARBER:</p> <p>24 Q. Do you go to the talc data</p>
Page 483	Page 485
<p>1 body of literature that I've or --</p> <p>2 is that what you'd like me to</p> <p>3 assume as well?</p> <p>4 BY MS. GARBER:</p> <p>5 Q. What I want you to assume is</p> <p>6 that one of your patients is asking you</p> <p>7 is it safe or not.</p> <p>8 A. But this is your world. And</p> <p>9 this is your hypothetical situation, so I</p> <p>10 want to make sure I'm doing it right.</p> <p>11 The patient is asking me,</p> <p>12 talcum powder products by Johnson &</p> <p>13 Johnson has fibrous talc as you said.</p> <p>14 And I'm just asking you, can I assume</p> <p>15 that the body of literature in its</p> <p>16 totality that I've reviewed is the same</p> <p>17 product that you're describing, there is</p> <p>18 no reason for me to have a different</p> <p>19 conversation?</p> <p>20 Q. My hypothetical did not</p> <p>21 include the body of literature.</p> <p>22 My hypothetical was that</p> <p>23 Johnson & Johnson's products contain</p> <p>24 fibrous talc and your patient is asking</p>	<p>1 because you make an assumption that</p> <p>2 Johnson & Johnson's products contain</p> <p>3 asbestos?</p> <p>4 MS. CURRY: Object to the</p> <p>5 form.</p> <p>6 THE WITNESS: I'm not sure</p> <p>7 what would make you say that.</p> <p>8 How else can I advise a</p> <p>9 patient on the risk of a substance</p> <p>10 without going to the epidemiologic</p> <p>11 data on that substance? She's</p> <p>12 asking me about talc. What other</p> <p>13 data am I going to review to give</p> <p>14 her an answer?</p> <p>15 BY MS. GARBER:</p> <p>16 Q. Doctor, you didn't look at</p> <p>17 the NTP data, did you?</p> <p>18 A. No.</p> <p>19 MS. GARBER: Okay. Let's</p> <p>20 just take a break and let me look</p> <p>21 at my notes. But I think I'm</p> <p>22 finished.</p> <p>23 MS. CURRY: Let's go off the</p> <p>24 record.</p>

Kevin Holcomb, M.D.

Page 486	Page 488
<p>1 THE VIDEOGRAPHER: Okay. 2 The time is 6:13 p.m. Off the 3 record. 4 (Short break.) 5 THE VIDEOGRAPHER: We are 6 back on the record. The time is 7 6:36 p.m. 8 BY MS. GARBER: 9 Q. Doctor, I'm going to mark an 10 additional paper that appears in the 11 Lancet dated March 23, 2019. 12 (Document marked for 13 identification as Exhibit 14 Holcomb-28.) 15 BY MS. GARBER: 16 Q. And, Doctor, you have not 17 seen this paper before, have you? 18 A. No. 19 Q. All right. If I could turn 20 your attention to the left-hand column 21 that appears at the bottom if you look up 22 here? 23 A. Yes. 24 Q. Okay. And, Doctor, it</p>	<p>1 some reason separated that one out 2 with a potentially. 3 BY MS. GARBER: 4 Q. All right. And the footnote 5 that the authors are citing to is the 6 Penninkilampi data, correct? 7 A. Yes. 8 Q. And, Doctor, I'm going to 9 mark another document as Exhibit 29. 10 (Document marked for 11 identification as Exhibit 12 Holcomb-29.) 13 BY MS. GARBER: 14 Q. And this is a study that 15 appeared in ACOG Obstetrics and 16 Gynecology, and it's titled "What's New 17 in Ovarian Cancer." 18 Do you see that? 19 A. Yes, I do. 20 Q. And it says, "Best articles 21 from the past year," correct? 22 A. Yes. 23 Q. It's written by Jason D. 24 Wright, M.D., correct?</p>
Page 487	Page 489
<p>1 reads -- the title is "Epithelial Ovarian 2 Cancer" by Stephanie -- oh boy. Okay. I 3 have to start with French. 4 A. Lheureux, I believe. 5 Q. Lheureux. All right. 6 And it indicates: "Risk 7 factors for epithelial ovarian cancer 8 include the number of lifetime ovulations 9 (absence of pregnancy, early age of 10 menarche, and late age of menarche) 11 family history of EOC, smoking, benign 12 gynecologic conditions (including 13 endometriosis, polycystic ovarian system, 14 and pelvic inflammatory disease) and 15 potentially the use of talcum powder." 16 Did I read that correctly? 17 A. Yes, you did. 18 Q. So here the authors just 19 days ago are indicating the potential of 20 talc as a risk factor for epithelial 21 ovarian cancer, true? 22 MS. CURRY: Object to the 23 form. 24 THE WITNESS: Yes. They for</p>	<p>1 A. Correct. 2 Q. You respect him? 3 A. Yes. 4 Q. And the Penninkilampi 5 article is listed as four of the best 6 articles from the past year, correct? 7 A. Yes. 8 Q. Doctor, we -- 9 MS. CURRY: Object to the 10 form of the last question. 11 THE WITNESS: I don't -- you 12 know, I'm sorry. 13 BY MS. GARBER: 14 Q. Doctor, I didn't have a 15 question. 16 A. No, no, I want to go back. 17 Because I said yes. But you made a few 18 misstatements there. 19 A, you said this was a 20 study. It's not. It's another op Ed 21 piece from Jason Wright saying what he 22 felt was the best papers of the year. 23 Two, you said it was an 24 ACOG. No, it's the journal of</p>

123 (Pages 486 to 489)

Kevin Holcomb, M.D.

Page 490	Page 492
<p>1 obstetrics -- Obstetrics and Gynecology 2 is the name of the journal this is in. 3 And just to clarify, without 4 speaking to Dr. Wright, I'm not sure why 5 he's calling these specifically the best, 6 whether he's speaking towards the quality 7 of the studies or just what's the most 8 popular or sensational. 9 Q. Doctor, what's the journal 10 name? 11 A. Obstetrics and Gynecology. 12 Q. Does that -- do people refer 13 to that as by a particular color? 14 A. Green. 15 Q. And that's a -- that's a 16 journal that you regularly read? 17 A. Yes. 18 Q. And you do some review work 19 for them, don't you? 20 A. Yes. 21 Q. That is a published document 22 that appears within the Green Journal, 23 right? 24 A. Yes. You're telling me this</p>	<p>1 exhaustive review haven't seen 2 before. 3 And so in that setting, if 4 there was some convincing data 5 that bumped them from 2-B to 1, 6 yes, I would feel differently 7 about it. 8 BY MS. GARBER: 9 Q. I will state in my 10 hypothetical that the IARC authors or 11 working group look at the data that 12 exists today with regard to the 13 epidemiological data, the meta-analyses 14 that exist, the nine meta-analyses, 15 including Taher, and the other 16 epidemiological data, the Saed data and 17 the other biologically plausible data, 18 and the mechanistic data that was 19 previously contained in IARC 2010, and 20 they concluded that it -- that talcum 21 powder products were a Group 1 22 carcinogen, would your opinions in this 23 matter change? 24 MS. CURRY: Object to the</p>
Page 491	Page 493
<p>1 is from the Green Journal, so it's -- 2 Q. Doctor, were you aware that 3 IARC is currently evaluating talcum 4 powder products for its carcinogenicity? 5 MS. CURRY: Object to the 6 form. 7 THE WITNESS: No. I was not 8 aware. 9 BY MS. GARBER: 10 Q. You are not aware of that? 11 Doctor, if -- I want you to 12 assume that IARC reviews the data that 13 exists to date and concludes that talcum 14 powder products are a Group 1 carcinogen. 15 Would your opinions in this case differ 16 with regard to talcum powder products? 17 MS. CURRY: Object to the 18 form. 19 THE WITNESS: I'd have to 20 see what additional data happened 21 between 2010 and 2019 that that 22 bumped them from 2-B to 1. So I'm 23 assuming that there would be some 24 data that I've -- after my</p>	<p>1 form. 2 THE WITNESS: I have to be 3 honest. It's hard for me to 4 imagine that Dr. Saed's paper 5 being quoted in IARC. So this is 6 a tough one for me to get into 7 your hypothetical situation here. 8 But no, I'm not so sure, 9 because I'm thinking from the last 10 time they published a 11 classification to now, there's 12 going to be three prospective 13 studies, all coming to the 14 conclusion that there is no 15 increased risk. 16 And then there's going to be 17 a number of meta-analysis, as 18 you're saying, which a lot of the 19 data is rechurning what they've 20 already looked at. So it would be 21 what incremental data have they 22 added to it. 23 So I guess I'm having a hard 24 time in your -- in your scenario,</p>

124 (Pages 490 to 493)

Kevin Holcomb, M.D.

Page 494	Page 496
<p>1 how IARC is going to get from a 2 2-B to a 1, based on what's been 3 published from the last time that 4 they issued an opinion on this. 5 BY MS. GARBER: 6 Q. I want you to assume that 7 they get to a 1. Is your opinion going 8 to change out of your respect for the 9 institution of IARC, a branch of the 10 World Health Organization? 11 MS. CURRY: Object to the 12 form. 13 THE WITNESS: If IARC used 14 Penninkilampi, for example -- 15 let's say that I was -- I'm going 16 to give you a hypothetical. 17 BY MS. GARBER: 18 Q. Doctor, you don't give me a 19 hypothetical. 20 A. If -- 21 Q. I give you one. You 22 understand that, right? 23 A. I'm giving you the 24 hypothetical of how I'm considering your</p>	<p>1 Q. Sure. Are you aware that 2 the FDA -- are you aware of FDA's 3 statements with regard to certain 4 cosmetic makeup products that are sold at 5 Justice and Claire's with regard to talc 6 and asbestos? 7 MS. CURRY: Object to the 8 form. 9 THE WITNESS: No, I'm not 10 aware. 11 BY MS. GARBER: 12 Q. Did you, before you came 13 here today and in preparation for your 14 deposition, endeavor to look at what FDA 15 is saying about talcum powder products? 16 MS. CURRY: Object to the 17 form. 18 THE WITNESS: No. 19 (Document marked for 20 identification as Exhibit 21 Holcomb-30.) 22 BY MS. GARBER: 23 Q. Let's mark this as 24 Exhibit 30.</p>
Page 495	Page 497
<p>1 situation. 2 Q. I want you to answer my 3 hypothetical. 4 A. It depends on what brought 5 them from 2-B to 1. I have respect for 6 IARC because I looked at their 7 methodology. We've gone through the 8 things that I didn't agree with IARC 9 methodology. But if you told me IARC's 10 quality dropped to such a standard that 11 they had Dr. Saed's paper as highly 12 credible, and this is moving us from here 13 to here, I'm no longer so impressed with 14 IARC. 15 So, no, my respect level for 16 IARC would drop considerably, and I 17 probably wouldn't follow the 18 recommendations. 19 Q. Doctor, you're aware, aren't 20 you, of FDA's recent statements with 21 regard to the businesses Justice and 22 Claire and their cosmetic products? 23 A. That's -- I'm not -- can you 24 repeat that once again.</p>	<p>1 Doctor, this is -- at the 2 bottom, you see this is the FDA's 3 website, right, FDA.gov/cosmetics? 4 A. Yes. 5 Q. Do you see that? 6 A. Yes. 7 Q. And do you see at the top it 8 indicates recalls and alerts? "FDA 9 advises consumers to stop using certain 10 Claire's cosmetic products." 11 Do you see that? 12 A. Yes. 13 Q. And do you see there in the 14 middle of the document, it indicates, 15 "Product samples test positive for 16 asbestos," and then it lists a number of 17 Claire's products? 18 A. Yes. 19 Q. Doctor, if there was such a 20 finding by FDA with regard to J&J's 21 talcum powder products, would your 22 opinions change in this case? 23 MS. CURRY: Object to the 24 form.</p>

Kevin Holcomb, M.D.

<p style="text-align: right;">Page 498</p> <p>1 THE WITNESS: I'd have to</p> <p>2 say the testing of the products</p> <p>3 that went into this body of</p> <p>4 knowledge that I have, I'm not</p> <p>5 sure. I would have to think about</p> <p>6 it. The reason why I'm hesitating</p> <p>7 is because I don't know, is that a</p> <p>8 new problem? Like, for example,</p> <p>9 this one store, Claire's stores, I</p> <p>10 think it's easier to call these</p> <p>11 folks out because you don't know</p> <p>12 if this is a new contamination.</p> <p>13 The question would be if all</p> <p>14 this data is with the same</p> <p>15 contaminated product, I'd have to</p> <p>16 assume that a woman is at no more</p> <p>17 increased risk than -- than --</p> <p>18 than the stuff in this paper -- in</p> <p>19 these papers.</p> <p>20 But I can't see myself going</p> <p>21 against FDA regulations. I mean,</p> <p>22 if FDA says stop using something,</p> <p>23 I'm not going to tell people to</p> <p>24 use something against FDA's</p>	<p style="text-align: right;">Page 500</p> <p>1 Q. You would heed the warning?</p> <p>2 MS. CURRY: Object to the</p> <p>3 form.</p> <p>4 THE WITNESS: I would think</p> <p>5 anyone with common sense would.</p> <p>6 It doesn't make sense to not to.</p> <p>7 BY MS. GARBER:</p> <p>8 Q. Similarly, if FDA compelled</p> <p>9 a warning to be placed on Johnson &</p> <p>10 Johnson's products, would you heed that</p> <p>11 warning if your patients were asking you</p> <p>12 if it was safe to use?</p> <p>13 MS. CURRY: Object to the</p> <p>14 form.</p> <p>15 THE WITNESS: Putting a</p> <p>16 warning on it or pulling it off</p> <p>17 the market?</p> <p>18 BY MS. GARBER:</p> <p>19 Q. Putting a warning on the</p> <p>20 bottle.</p> <p>21 MS. CURRY: Object to the</p> <p>22 form.</p> <p>23 THE WITNESS: Would I tell</p> <p>24 patients to heed the warning.</p>
<p style="text-align: right;">Page 499</p> <p>1 regulations.</p> <p>2 BY MS. GARBER:</p> <p>3 Q. And if FDA indicates that</p> <p>4 the testing that they conducted of</p> <p>5 Johnson & Johnson's talcum powder</p> <p>6 products test positive for asbestos,</p> <p>7 would your causation opinions change?</p> <p>8 MS. CURRY: Object to the</p> <p>9 form.</p> <p>10 THE WITNESS: No. No.</p> <p>11 BY MS. GARBER:</p> <p>12 Q. Would your advice to</p> <p>13 patients change?</p> <p>14 A. Apparently the FDA would</p> <p>15 likely put out a warning to say stop</p> <p>16 using it, and, yeah, I would stop using</p> <p>17 it. I've done that in the past where</p> <p>18 there's things that -- if the FDA sends</p> <p>19 out a warning about, and I stop doing it,</p> <p>20 even though I may think in my hands it's</p> <p>21 safe.</p> <p>22 It has a lot to do with</p> <p>23 medical/legal issues and things like</p> <p>24 that. But --</p>	<p style="text-align: right;">Page 501</p> <p>1 BY MS. GARBER:</p> <p>2 Q. Sure. If the patient -- if</p> <p>3 there was a warning about ovarian cancer</p> <p>4 on the bottle, compelled by -- by FDA and</p> <p>5 your patient came and said I've been</p> <p>6 putting this on my genitals, should I</p> <p>7 stop, what would your answer be?</p> <p>8 MS. CURRY: Object to the</p> <p>9 form.</p> <p>10 THE WITNESS: I have to</p> <p>11 believe that if the -- if the FDA</p> <p>12 thought that that product was such</p> <p>13 a carcinogen and so dangerous</p> <p>14 there wouldn't be just a warning</p> <p>15 label, they would pull it off the</p> <p>16 market. If the FDA is just</p> <p>17 putting a warning so that patients</p> <p>18 are aware of it, I think my</p> <p>19 conversation with her is going to</p> <p>20 be very similar to the</p> <p>21 conversation I just told you I</p> <p>22 would have now.</p> <p>23 BY MS. GARBER:</p> <p>24 Q. But you wouldn't tell her</p>

Kevin Holcomb, M.D.

Page 502	Page 504
<p>1 to -- to stop using it?</p> <p>2 A. My guess is the warning</p> <p>3 would be very similar to the</p> <p>4 conversations I'm having, there are some</p> <p>5 weaker data suggesting -- so in your --</p> <p>6 you know, your hypothetical situation,</p> <p>7 it's -- I would think that they would</p> <p>8 possibly recall it or -- not recall it.</p> <p>9 They would -- they would put an advice to</p> <p>10 stop using a certain product, like they</p> <p>11 are doing in this situation. And a</p> <p>12 patient came to me and says the FDA has</p> <p>13 this warning to stop using this product,</p> <p>14 I would support the FDA.</p> <p>15 Q. And, Doctor, I know you are</p> <p>16 not a regulatory expert, but you do know</p> <p>17 that at times FDA does not have the power</p> <p>18 to compel a warning, you understand that,</p> <p>19 right?</p> <p>20 A. I -- I, really -- as you</p> <p>21 started with your statement, I am not a</p> <p>22 regulatory expert. I know very little</p> <p>23 about regulations and how the FDA works</p> <p>24 in that regard.</p>	<p>1 to investigate and monitor reports of</p> <p>2 asbestos contamination in certain</p> <p>3 cosmetic products and will provide</p> <p>4 additional information as it becomes</p> <p>5 available. The agency is and will</p> <p>6 continue to work with other" -- "other</p> <p>7 federal partners to share our collective</p> <p>8 expertise to advance scientific test</p> <p>9 methods for the assessment of asbestos."</p> <p>10 Did I read that correctly?</p> <p>11 A. So far you've been perfect.</p> <p>12 Q. Does it cause you concern</p> <p>13 that the FDA is interested in looking</p> <p>14 further into whether talcum powder</p> <p>15 products contain asbestos?</p> <p>16 MS. CURRY: Object to the</p> <p>17 form.</p> <p>18 THE WITNESS: No. It</p> <p>19 actually gives me reassurance that</p> <p>20 the federal agencies that are</p> <p>21 supposed to be protecting public</p> <p>22 safety are at work and doing what</p> <p>23 they are supposed to be doing.</p> <p>24 BY MS. GARBER:</p>
Page 503	Page 505
<p>1 (Document marked for</p> <p>2 identification as Exhibit</p> <p>3 Holcomb-31.)</p> <p>4 BY MS. GARBER:</p> <p>5 Q. I want to mark another</p> <p>6 document. And this is Exhibit 31, which</p> <p>7 is from the FDA website. And it's titled</p> <p>8 "Talc."</p> <p>9 Doctor, do you see -- do you</p> <p>10 see that the date of the download of this</p> <p>11 document is March 19, 2019?</p> <p>12 A. Yes.</p> <p>13 Q. And, Doctor, did you ever</p> <p>14 endeavor to go to the FDA website and put</p> <p>15 in "talc" to see what the FDA was saying</p> <p>16 about talcum powder products?</p> <p>17 A. No.</p> <p>18 Q. Okay. I will represent to</p> <p>19 you what appears new on this website is</p> <p>20 what's under the heading of "Talc."</p> <p>21 It says, "Here is a recent</p> <p>22 FDA action related to talc. Learn more</p> <p>23 below."</p> <p>24 It reads, "The FDA continues</p>	<p>1 Q. But you are here in this</p> <p>2 litigation saying talc is safe, even</p> <p>3 though FDA is looking into whether or not</p> <p>4 talcum powder products contain asbestos.</p> <p>5 A. Right. So if --</p> <p>6 MS. CURRY: Object to the</p> <p>7 form.</p> <p>8 BY MS. GARBER:</p> <p>9 Q. It doesn't concern you?</p> <p>10 A. It would concern me if they</p> <p>11 told me that they found levels of talc</p> <p>12 and -- and -- you know, the -- the reason</p> <p>13 why it would concern me is because I</p> <p>14 don't know if that's a new contamination</p> <p>15 or that product is the same as it's</p> <p>16 always been.</p> <p>17 If it's the same as it's</p> <p>18 always been, then you are talking about a</p> <p>19 level of contamination that doesn't have</p> <p>20 compelling evidence that it causes</p> <p>21 cancer.</p> <p>22 But I don't know how I would</p> <p>23 know the difference. I think I would</p> <p>24 have to assume that it's -- that it's</p>

Kevin Holcomb, M.D.

Page 506	Page 508
<p>1 different than this. I think you'd have 2 to either assume it's the same or it's 3 different. And I think the safer thing 4 to do would be to assume that it's 5 different. 6 If I knew for sure that this 7 level of contamination they find has been 8 in this stuff all this time and all these 9 thousands of patients that we've 10 followed, you know, the large 11 case-control studies, the 70,000, 60,000, 12 40,000 patients on cohort studies, if 13 that's the product that they've been 14 using and it's contaminated all this 15 time, I would have to say no, that 16 wouldn't worry me. But there's no way 17 that I would be able to tell the 18 difference. 19 Q. Shouldn't you, as a patient 20 advocate, err on the side of safety? 21 MS. CURRY: Object to the 22 form. 23 THE WITNESS: That's what I 24 just said, I would.</p>	<p>1 THE WITNESS: You're saying 2 the advisory would just say that 3 there's some evidence suggesting 4 that talc -- what is the -- can 5 you word the -- can you give me 6 the hypothetical wording of what 7 is SGO is saying? 8 BY MS. GARBER: 9 Q. Sure. SGO has issued an 10 advisory that says there is evidence that 11 talc can cause cancer, ovarian cancer. 12 A. Right. And then -- 13 Q. Would you -- would you 14 continue to advise patients that talcum 15 powder products are safe? 16 MS. CURRY: Object to the 17 form. 18 THE WITNESS: Before I made 19 a decision on that I'd have to go 20 and see what is the data that they 21 are basing that on. 22 If they are basing it on the 23 data that I've just reviewed, I 24 would have the same discussion</p>
Page 507	Page 509
<p>1 BY MS. GARBER: 2 Q. You know, Doctor, if -- you 3 are a member of the SGO, right? 4 A. Yes. 5 Q. And that stands for Society 6 of Gynecologic Oncology, right? 7 A. Yes. 8 Q. That's a professional 9 organization? 10 A. Yes. 11 Q. And do you know what -- 12 whether they list talc as a risk factor 13 at present? 14 A. On which site, on the SGO 15 website? 16 Q. Yeah. 17 A. No, I'm not -- I'm not sure. 18 Q. I want you to assume that -- 19 that the SGO issues an advisory that talc 20 can cause cancer. Would you continue to 21 recommend to patients that they use 22 talcum powder products on their genitals? 23 MS. CURRY: Object to the 24 form.</p>	<p>1 with my patients, because I -- I 2 would say them saying that there's 3 evidence to this effect is just 4 telling the truth. 5 If I then have to go and 6 read the body of literature that 7 they're using to make that 8 warning, to decide, well, yes, 9 the -- the studies that they are 10 referring to are the same ones I 11 know, and the ones that don't is 12 the same amount going both ways, 13 my feeling would be the same. 14 So is their advisory based 15 on new data or an assessment of 16 what I've assessed? 17 BY MS. GARBER: 18 Q. You wouldn't heed the 19 advisory of the SGO, your professional 20 organization, is that your testimony? 21 A. And stop using talc myself? 22 What -- what would -- 23 MS. CURRY: Object to the 24 form.</p>

Kevin Holcomb, M.D.

<p style="text-align: right;">Page 510</p> <p>1 BY MS. GARBER: 2 Q. And advise patients that 3 it's safe to use? 4 A. You didn't say that SGO is 5 advising to stop using talc. You said 6 what would I do if the SGO had an 7 advisory just saying that patients should 8 be aware that there's information out 9 there to this effect. 10 Q. That wasn't my hypothetical, 11 was it, Doctor? 12 A. Yeah. Can you go back and 13 read it? 14 Q. The SGO issues an advisory 15 that talc can cause cancer. Would that 16 change what you told patients about the 17 safety of talcum powder products? 18 MS. CURRY: Object to the 19 form. 20 THE WITNESS: If the SGO 21 jumped up to the same 22 classification as IARC that says 23 there's insufficient evidence but 24 this is potentially a carcinogen,</p>	<p style="text-align: right;">Page 512</p> <p>1 Q. You're not going to heed the 2 advisory of the SGO? 3 MS. CURRY: Object to the 4 form. 5 THE WITNESS: You -- the 6 advice -- 7 BY MS. GARBER: 8 Q. Because you know the data 9 better? 10 A. The advice -- there is no 11 advisory here. You keep on saying that 12 the SGO is saying that there's evidence 13 that talc can cause cancer. An advisory 14 is telling you to do something. In this 15 case, are they saying stop using talc or 16 that patients should just be aware? 17 Q. Let me give you another 18 hypothetical. SGO issues an advisory to 19 stop using talcum powder products on your 20 genitals because it contains asbestos. 21 Would you heed that advisory? 22 MS. CURRY: Object to the 23 form. 24 THE WITNESS: If the SGO is</p>
<p style="text-align: right;">Page 511</p> <p>1 I don't see how SGO would be 2 saying anything different than 3 IARC. 4 So that -- that statement 5 that says it can, you'd have to go 6 in and see, well, what's the 7 evidence that you're basing it on. 8 And I'm saying that -- why 9 would I change my feeling about 10 this if somebody else looks at 11 this data, and it's the same data 12 that I've just reviewed, and says 13 we're going to make this 14 statement. 15 And the patient comes to me 16 and asks me, well, how do you feel 17 about that statement? And if it's 18 based on this same data, I'm not 19 sure how it changes the fact that 20 it's from SGO. I'm still going to 21 then explain, this is the truth as 22 I see it and the totality of the 23 evidence. 24 BY MS. GARBER:</p>	<p style="text-align: right;">Page 513</p> <p>1 telling patients to stop using 2 talc because of asbestos that's 3 been proven to be there, yes, to 4 be honest, I would probably drop 5 in line, just not to be out of -- 6 I'd be fearing medical/legal 7 exposure by not doing it, no 8 matter how I felt about the data. 9 BY MS. GARBER: 10 Q. More concerned about your 11 neck rather than the patients, Doctor? 12 MS. CURRY: Object to the 13 form. 14 THE WITNESS: I have my 15 opinion of this data. The data -- 16 if you're saying my hypothetical 17 that I just gave you is that the 18 data didn't change and SGO makes a 19 statement. I'm worried about the 20 patients the same amount, because 21 the data is the data. 22 You're saying, well, what if 23 SGO gets behind it and says based 24 on what you read, we want to give</p>

Kevin Holcomb, M.D.

Page 514	Page 516
<p>1 an advisory?</p> <p>2 The risk level hasn't</p> <p>3 changed. It's not based on any</p> <p>4 new data. So I don't care about</p> <p>5 my patients any less. The risk to</p> <p>6 them hasn't increased.</p> <p>7 BY MS. GARBER:</p> <p>8 Q. Doctor, is cornstarch a safe</p> <p>9 alternative to talcum powder products?</p> <p>10 MS. CURRY: Object to the</p> <p>11 form.</p> <p>12 THE WITNESS: It's an</p> <p>13 alternative, yes.</p> <p>14 BY MS. GARBER:</p> <p>15 Q. Is it a safe alternative?</p> <p>16 MS. CURRY: Object to the</p> <p>17 form.</p> <p>18 THE WITNESS: I have no</p> <p>19 reason to think that cornstarch is</p> <p>20 not safe.</p> <p>21 BY MS. GARBER:</p> <p>22 Q. You haven't done a</p> <p>23 comprehensive literature review of the</p> <p>24 cornstarch data, have you?</p>	<p>1 finished.</p> <p>2 THE VIDEOGRAPHER: Okay.</p> <p>3 Stand by, please. This marks the</p> <p>4 end of today's deposition. The</p> <p>5 time is 6:59 p.m.</p> <p>6 (Excused.)</p> <p>7 (Deposition concluded at</p> <p>8 approximately 6:59 p.m.)</p> <p>9</p> <p>10</p> <p>11</p> <p>12</p> <p>13</p> <p>14</p> <p>15</p> <p>16</p> <p>17</p> <p>18</p> <p>19</p> <p>20</p> <p>21</p> <p>22</p> <p>23</p> <p>24</p>
Page 515	Page 517
<p>1 A. No.</p> <p>2 Q. Let me ask you about some of</p> <p>3 the expert work that you've done, just so</p> <p>4 that I'm clear on your prior testimony.</p> <p>5 Since the Ingham case, and</p> <p>6 that verdict, and before you were hired</p> <p>7 in the MDL, did you continue to do any</p> <p>8 expert work with regard to talcum powder</p> <p>9 products and ovarian cancer?</p> <p>10 A. No. You actually asked me</p> <p>11 that earlier. Same answer. No.</p> <p>12 Q. Okay. And are you currently</p> <p>13 serving as an expert on the talcum powder</p> <p>14 products in any other litigation aside</p> <p>15 from the MDL?</p> <p>16 A. No.</p> <p>17 MS. GARBER: Okay. Just</p> <p>18 give me one moment.</p> <p>19 Okay. All right. I have</p> <p>20 nothing further at this point.</p> <p>21 Thank you, Doctor.</p> <p>22 THE WITNESS: Sure.</p> <p>23 MS. CURRY: No questions.</p> <p>24 MS. GARBER: Okay. We're</p>	<p>1</p> <p>2 CERTIFICATE</p> <p>3</p> <p>4</p> <p>5 I HEREBY CERTIFY that the</p> <p>6 witness was duly sworn by me and that the</p> <p>7 deposition is a true record of the</p> <p>8 testimony given by the witness.</p> <p>9</p> <p>10 It was requested before</p> <p>11 completion of the deposition that the</p> <p>12 witness, KEVIN HOLCOMB, M.D. have the</p> <p>13 opportunity to read and sign the</p> <p>14 deposition transcript.</p> <p>15</p> <p>16</p> <p>17</p> <p>18</p> <p>19</p> <p>20</p> <p>21</p> <p>22</p> <p>23</p> <p>24</p> <p>25</p> <p>26</p> <p>27</p> <p>28</p> <p>29</p> <p>30</p> <p>31</p> <p>32</p> <p>33</p> <p>34</p> <p>35</p> <p>36</p> <p>37</p> <p>38</p> <p>39</p> <p>40</p> <p>41</p> <p>42</p> <p>43</p> <p>44</p> <p>45</p> <p>46</p> <p>47</p> <p>48</p> <p>49</p> <p>50</p> <p>51</p> <p>52</p> <p>53</p> <p>54</p> <p>55</p> <p>56</p> <p>57</p> <p>58</p> <p>59</p> <p>60</p> <p>61</p> <p>62</p> <p>63</p> <p>64</p> <p>65</p> <p>66</p> <p>67</p> <p>68</p> <p>69</p> 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<p>618</p> <p>619</p> <p>620</p> <p>621</p> <p>622</p> <p>623</p> <p>624</p> <p>625</p> <p>626</p> <p>627</p> <p>628</p> <p>629</p> <p>630</p> <p>631</p> <p>632</p> <p>633</p> <p>634</p> <p>635</p> <p>636</p> <p>637</p> <p>638</p> <p>639</p> <p>640</p> <p>641</p> <p>642</p> <p>643</p> <p>644</p> <p>645</p> <p>646</p> <p>647</p> <p>648</p> <p>649</p> <p>650</p> <p>651</p> <p>652</p> <p>653</p> <p>654</p> <p>655</p> <p>656</p> <p>657</p> <p>658</p> <p>659</p> <p>660</p> <p>661</p> <p>662</p> <p>663</p> <p>664</p> <p>665</p> <p>666</p> <p>667</p> <p>668</p> <p>669</p> <p>670</p> <p>671</p> <p>672</p> <p>673</p> <p>674</p> <p>675</p> <p>676</p> <p>677</p> <p>678</p> <p>679</p> <p>680</p> <p>681</p> <p>682</p> <p>683</p> <p>684</p> <p>685</p> <p>686</p> <p>687</p> <p>688</p> <p>689</p> <p>690</p> <p>691</p> <p>692</p> <p>693</p> <p>694</p> <p>695</p> <p>696</p> <p>697</p> <p>698</p> <p>699</p> <p>700</p> <p>701</p> <p>702</p> <p>703</p> <p>704</p> <p>705</p> <p>706</p> <p>707</p> <p>708</p> <p>709</p> <p>710</p> <p>711</p> <p>712</p> <p>713</p> <p>714</p> <p>715</p> <p>716</p> <p>717</p> <p>718</p> <p>719</p> <p>720</p> <p>721</p> <p>722</p> <p>723</p> <p>724</p> <p>725</p> <p>726</p> <p>727</p> <p>728</p> <p>729</p> <p>730</p> <p>731</p> <p>732</p> <p>733</p> <p>734</p> <p>735</p> <p>736</p> <p>737</p> <p>738</p> <p>739</p> <p>740</p> <p>741</p> <p>742</p> <p>743</p> <p>744</p> <p>745</p> <p>746</p> <p>747</p> <p>748</p> <p>749</p> <p>750</p> <p>751</p> <p>752</p> <p>753</p> <p>754</p> <p>755</p> <p>756</p> <p>757</p> <p>758</p> <p>759</p> <p>760</p> <p>761</p> <p>762</p> <p>763</p> <p>764</p> <p>765</p> <p>766</p> <p>767</p> <p>768</p> <p>769</p> <p>770</p> <p>771</p> <p>772</p> <p>773</p> <p>774</p> <p>775</p> <p>776</p> <p>777</p> <p>778</p> <p>779</p> <p>780</p> <p>781</p> <p>782</p> <p>783</p> <p>784</p> <p>785</p> <p>786</p> <p>787</p> <p>788</p> <p>789</p> <p>790</p> <p>791</p> <p>792</p> <p>793</p> <p>794</p> <p>795</p> <p>796</p> <p>797</p> <p>798</p> <p>799</p> <p>800</p> <p>801</p> <p>802</p> <p>803</p> <p>804</p> <p>805</p> <p>806</p> <p>807</p> <p>808</p> <p>809</p> <p>810</p> <p>811</p> <p>812</p> <p>813</p> <p>814</p> <p>815</p> <p>816</p> <p>817</p> <p>818</p> <p>819</p> <p>820</p> <p>821</p> <p>822</p> <p>823</p> <p>824</p> <p>825</p> <p>826</p> <p>827</p> <p>828</p> <p>829</p> <p>830</p> <p>831</p> <p>832</p> <p>833</p> <p>834</p> <p>835</p> <p>836</p> <p>837</p> <p>838</p> <p>839</p> <p>840</p> <p>841</p> <p>842</p> <p>843</p> <p>844</p> <p>845</p> <p>846</p> <p>847</p> <p>848</p> <p>849</p> <p>850</p> <p>851</p> <p>852</p> <p>853</p> <p>854</p> <p>855</p> <p>856</p> <p>857</p> <p>858</p> <p>859</p> <p>860</p> <p>861</p> <p>862</p> <p>863</p> <p>864</p> <p>865</p> <p>866</p> <p>867</p> <p>868</p> <p>869</p> <p>870</p> <p>871</p> <p>872</p> <p>873</p> <p>874</p> <p>875</p> <p>876</p> <p>877</p> <p>878</p> <p>879</p> <p>880</p> <p>881</p> <p>882</p> <p>883</p> <p>884</p> <p>885</p> <p>886</p> <p>887</p> <p>888</p> <p>889</p> <p>890</p> <p>891</p> <p>892</p> <p>893</p> <p>894</p> <p>895</p> <p>896</p> <p>897</p> <p>898</p> <p>899</p> <p>900</p> <p>901</p> <p>902</p> <p>903</p> <p>904</p> <p>905</p> <p>906</p> <p>907</p> <p>908</p> <p>909</p> <p>910</p> <p>911</p> <p>912</p> <p>913</p> <p>914</p> <p>915</p> <p>916</p> <p>917</p> <p>918</p> <p>919</p> <p>920</p> <p>921</p> <p>922</p> <p>923</p> <p>924</p> <p>925</p> <p>926</p> <p>927</p> <p>928</p> <p>929</p> <p>930</p> <p>931</p> <p>932</p> <p>933</p> <p>934</p> <p>935</p> <p>936</p> <p>937</p> <p>938</p> <p>939</p> <p>940</p> <p>941</p> <p>942</p> <p>943</p> <p>944</p> <p>945</p> <p>946</p> <p>947</p> <p>948</p> <p>949</p> <p>950</p> <p>951</p> <p>952</p> <p>953</p> <p>954</p> <p>955</p> <p>956</p> <p>957</p> <p>958</p> <p>959</p> <p>960</p> <p>961</p> <p>962</p> <p>963</p> <p>964</p> <p>965</p> <p>966</p> <p>967</p> <p>968</p> <p>969</p> <p>970</p> <p>971</p> <p>972</p> <p>973</p> <p>974</p> <p>975</p> <p>976</p> <p>977</p> <p>978</p> <p>979</p> <p>980</p> <p>981</p> <p>982</p> <p>983</p> <p>984</p> <p>985</p> <p>986</p> <p>987</p> <p>988</p> <p>989</p> <p>990</p> <p>991</p> <p>992</p> <p>993</p> <p>994</p> <p>995</p> <p>996</p> <p>997</p> <p>998</p> <p>999</p> <p>1000</p>

130 (Pages 514 to 517)

Kevin Holcomb, M.D.

Page 518	Page 520
<p>1 INSTRUCTIONS TO WITNESS</p> <p>2</p> <p>3 Please read your deposition</p> <p>4 over carefully and make any necessary</p> <p>5 corrections. You should state the reason</p> <p>6 in the appropriate space on the errata</p> <p>7 sheet for any corrections that are made.</p> <p>8 After doing so, please sign</p> <p>9 the errata sheet and date it.</p> <p>10 You are signing same subject</p> <p>11 to the changes you have noted on the</p> <p>12 errata sheet, which will be attached to</p> <p>13 your deposition.</p> <p>14 It is imperative that you</p> <p>15 return the original errata sheet to the</p> <p>16 deposing attorney within thirty (30) days</p> <p>17 of receipt of the deposition transcript</p> <p>18 by you. If you fail to do so, the</p> <p>19 deposition transcript may be deemed to be</p> <p>20 accurate and may be used in court.</p> <p>21</p> <p>22</p> <p>23</p> <p>24</p>	<p>1</p> <p>2 ACKNOWLEDGMENT OF DEPONENT</p> <p>3</p> <p>4 I, _____, do</p> <p>5 hereby certify that I have read the</p> <p>6 foregoing pages, 1 - 521, and that the</p> <p>7 same is a correct transcription of the</p> <p>8 answers given by me to the questions</p> <p>9 therein propounded, except for the</p> <p>10 corrections or changes in form or</p> <p>11 substance, if any, noted in the attached</p> <p>12 Errata Sheet.</p> <p>13</p> <p>14</p> <p>15 _____</p> <p>16 KEVIN HOLCOMB, M.D. DATE</p> <p>17</p> <p>18</p> <p>19 Subscribed and sworn</p> <p>20 to before me this</p> <p>21 _____ day of _____, 20 ____.</p> <p>22 My commission expires: _____</p> <p>23</p> <p>24 _____</p> <p>25 Notary Public</p>
Page 519	Page 521
<p>1 - - - - -</p> <p>2 E R R A T A</p> <p>3 - - - - -</p> <p>4 PAGE LINE CHANGE</p> <p>5 _____</p> <p>6 REASON: _____</p> <p>7 _____</p> <p>8 REASON: _____</p> <p>9 _____</p> <p>10 REASON: _____</p> <p>11 _____</p> <p>12 REASON: _____</p> <p>13 _____</p> <p>14 REASON: _____</p> <p>15 _____</p> <p>16 REASON: _____</p> <p>17 _____</p> <p>18 REASON: _____</p> <p>19 _____</p> <p>20 REASON: _____</p> <p>21 _____</p> <p>22 REASON: _____</p> <p>23 _____</p> <p>24 REASON: _____</p>	<p>1 LAWYER'S NOTES</p> <p>2 PAGE LINE</p> <p>3 _____</p> <p>4 _____</p> <p>5 _____</p> <p>6 _____</p> <p>7 _____</p> <p>8 _____</p> <p>9 _____</p> <p>10 _____</p> <p>11 _____</p> <p>12 _____</p> <p>13 _____</p> <p>14 _____</p> <p>15 _____</p> <p>16 _____</p> <p>17 _____</p> <p>18 _____</p> <p>19 _____</p> <p>20 _____</p> <p>21 _____</p> <p>22 _____</p> <p>23 _____</p> <p>24 _____</p>

131 (Pages 518 to 521)

A	276:13 277:23	318:14 346:8	248:12	345:14,15,20
a.m 1:15 11:7	352:9 397:24	352:2	afternoon	345:22 366:22
126:11,16	accounts 398:21	addressing	239:22	369:5 370:9
AACES 7:14	accuracy 371:3	28:21 158:21	age 340:18	388:4 398:8
abandoned	accurate 14:12	323:9 429:7	351:18 364:2	401:3,22 402:9
214:18	22:1 23:18	adenomatous	364:10,21	402:21 404:17
ability 17:8	110:24 117:1	456:6	368:20 383:24	410:1,17
95:11 116:9	124:4 151:7	adequate 345:7	444:10 487:9	425:19 427:12
131:17 135:17	303:24 355:24	adequately	487:10	430:15 432:20
282:3 285:7	380:15,18	399:15	aged 366:1,3	439:17 452:18
422:9 426:7	518:20	ADLs 251:6,6	agencies 504:20	455:9 457:10
able 77:14 78:18	accurately	administer	agency 504:5	459:4,13,14
79:1 130:3,11	318:1 369:4	11:17	agent 72:14	470:12 471:3
132:12 148:17	achieve 194:6	admit 130:24	74:17 469:16	479:14 495:8
159:5 168:15	acid 151:24	380:9	agents 445:10	agreed 182:15
199:8 216:8	acknowledge	admitted 91:4	ages 366:5	348:24
290:9,10	128:1 155:24	94:22	ago 47:12 55:21	agreeing 297:2
314:16,20	ACKNOWLEDGE...	admitting 42:8	86:21 88:1	agrees 292:6
318:1 321:8	520:2	133:4 294:6,8	111:12 140:19	ahead 31:9 54:1
339:17 396:24	ACOG 488:15	294:10,13	143:17 354:24	66:11 237:8
438:6 442:14	489:24	330:21	461:5 487:19	al 88:19,19
506:17	act 323:10	admonitions	agree 20:21	255:19 303:4
absence 131:7	action 275:12	15:2	32:11 41:23	358:4 416:11
315:2 427:9	276:9 447:3	adnexa 151:21	89:10 93:20,22	416:23,24
487:9	503:22	advance 504:8	96:5,8 101:15	417:5,15
absolute 396:11	activities 251:9	advanced 336:3	101:18 155:22	453:15,18
abstract 125:4	251:20	advice 499:12	157:9 158:23	462:10
329:15 383:19	activity 251:11	502:9 512:6,10	162:23 170:14	Alabama 2:14
404:11,23	264:12	advise 239:7	173:9 182:12	alerts 497:8
476:9	actual 122:11	315:9 485:8	182:18 184:11	ALLEN 2:12
absurd 204:1	400:16	508:14 510:2	212:14,15,19	allow 458:13
217:14	acute 450:21	advises 9:19	212:24 214:16	allowed 73:14
academic 178:2	add 81:3 110:22	497:9	215:11 216:11	154:20 163:22
Academy	329:1 373:3	advising 510:5	221:2,12	alter 283:20
446:19	added 229:1	advisory 507:19	222:23 223:2	alterations
accept 77:22,23	493:22	508:2,10	227:20 241:7	251:21
78:11 90:8	adding 291:23	509:14,19	247:4,13,14	altered 282:3
acceptable	addition 54:5	510:7,14 512:2	249:3,11,13,16	alternative
48:21	116:13 439:20	512:11,13,18	250:4 257:11	469:16 480:14
accepted 61:8	additional 54:8	512:21 514:1	257:18,18	514:9,13,15
151:8 196:4	88:6 486:10	advocate 238:18	258:6 295:14	altogether
295:8	491:20 504:4	238:23,24	297:14,20	219:19 220:2
access 299:20	address 23:14	239:4 506:20	298:23 299:4	290:22 311:20
accompany 15:2	26:6 273:5,10	affect 291:2	300:7 317:12	313:12 321:20
accord 219:3	273:13 309:8	affirmative	317:13 318:3	321:23
account 196:22	398:17	23:22	325:21 326:2	amend 300:8
	addressed 57:2	African 7:13	329:13 335:5	amendments

151:7	163:11,21	255:24	approximate	74:6,8,23
American 7:13	166:23 167:5	apparent 293:16	264:18 290:7	75:14 76:1
9:8	167:12,16	386:22	approximately	82:3,24 83:9
Americans	168:4 169:6,24	apparently	336:5 516:8	84:21 85:16,19
248:13	171:2 174:10	420:21 445:20	April 424:17	85:23 86:4,15
amount 39:13	176:13 191:3	499:14	428:6	87:19 88:9
137:9 264:12	205:24 213:14	appear 51:15	area 27:21 43:13	89:17 90:2,20
386:4 390:2	228:8,10,12,14	57:11 58:18	68:15 85:2	91:5,6 95:1,10
409:13 431:7	232:18 233:2	105:5 116:12	106:21 392:6	95:22 96:6,10
431:12 509:12	298:7 316:18	152:4,13,21,23	393:14 427:2	96:17,23 98:6
513:20	327:14,24	160:7 186:17	428:22 453:2	98:21 99:7,19
amphibole	330:11 353:12	appearances 2:1	areas 138:20	100:4,16
42:24	354:13 356:3	3:1 4:1 11:14	323:11 376:6	101:16,18
Amrhein 6:18	401:21 411:2	appeared	argue 166:4	108:19 109:23
analogies	415:1,3 458:4	488:15	253:4 266:23	154:15 170:8
120:13	458:14 485:14	appears 186:10	450:4	175:2 239:8
analysis 18:5	495:2 501:7	186:17 424:19	argument	326:17 330:10
34:7 171:7,18	515:11	471:19 476:17	460:14	342:19 391:5
171:21 189:14	answered 31:14	486:10,21	Arsenic 5:22	391:12 393:4
217:3 225:20	67:21 80:20	490:22 503:19	71:10	398:21 478:17
229:8 249:18	288:14	APPEL 3:17	article 182:2	479:3 480:24
278:20,20	answering	application 84:7	194:12 196:7	481:6,11,20,23
345:24 387:14	101:14 265:21	432:9 435:5	200:20 299:7,9	484:17 485:3
387:18 429:3	328:17 456:23	applications	299:18 300:9	496:6 497:16
431:15 436:6	answers 166:16	417:2	363:21 463:20	499:6 504:2,9
446:23 453:19	166:22 167:1	applied 145:12	489:5	504:15 505:4
477:15	411:6 520:8	427:4 428:12	articles 54:9	512:20 513:2
analyzing	anti-inflamma...	applies 85:21	120:23 217:3	ascend 445:15
428:20 430:8	459:6	86:15	287:4 488:20	ascending 423:4
and/or 14:14	anticipate 405:6	apply 75:15 76:2	489:6	ascension
113:19 517:21	antiinflammat...	85:17 484:1	asbestiform	127:23 131:10
Andrew 468:23	447:14,17	517:19	75:18 85:1,7	ascent 445:10
animal 127:22	449:8 455:12	appreciably	85:20,22 86:16	aside 52:23
129:4,8,13,19	455:19	270:11	89:18 95:1	111:5 207:9
130:11 131:9	antiinflammat...	appreciate	96:2,6 98:24	515:14
134:16	453:16 454:17	24:13 31:12	asbestos 22:13	asked 42:6
animals 134:17	anybody 37:5	126:7 209:1	22:16 26:15,19	43:11,17 46:14
anniversary	150:10 307:17	255:1 280:23	26:22 27:1,12	56:16 59:17
389:8	341:16,22	353:14 465:16	27:19 28:7	63:16,19 66:20
answer 10:5	451:20	appreciated	38:14,20 39:12	67:16 80:17
15:22 41:21	anyway 237:9	122:22	41:17,24 42:7	81:18 88:12
45:23 48:20	460:20	approach	42:9,13 60:14	97:6,6,17,18
59:3 63:20	apart 340:3	128:22 163:5	61:13,23 62:15	98:1 103:9
65:3,11 66:12	391:16	appropriate	62:22 63:18	106:3 138:19
67:17 68:7,8	apologize 40:19	168:5 223:22	65:1,6,8 67:8	138:20 141:2
91:21 99:10	71:13,20 72:1	463:3 473:15	67:22 68:1	143:22 144:11
133:16 136:8	87:10 232:21	473:16 518:6	69:18 70:24	144:20 145:1

178:18 182:15	assessing 20:13	484:11	283:9 300:15	218:11,24
189:7 190:15	157:11,13	associations	411:12	219:4 220:19
190:16 191:8	158:22	115:23 276:14	attempted 48:15	222:20 223:3
209:12 211:13	assessment 6:19	277:24	408:4	231:9 237:10
211:20 216:17	33:22 43:12	assume 16:6,19	attempting	237:19 247:17
228:9,15,24	90:19 142:14	76:4 98:5	296:15	253:17 254:4
286:20 306:14	145:24 220:11	108:16 177:1	attendant 44:10	257:19,24
314:13 328:2,9	252:9 257:19	177:22 178:8	115:6 146:16	259:19 261:4
328:17 332:3	345:17 376:15	217:5 218:2,24	154:7 181:2	267:3 272:14
341:21 348:21	420:11 428:19	243:1 265:18	288:21	273:7,7,14,15
353:9 366:18	436:7 477:19	323:16 331:16	attention 28:14	275:11 279:13
367:8 371:17	504:9 509:15	372:24 429:9	40:4 486:20	279:23 280:14
371:23,24	assigned 215:22	473:17 479:2	attenuated	287:14 309:1
372:10 376:8	assignment 43:8	482:10,22	78:16	334:10 344:11
384:3 413:6	43:20	483:3,5,14	attorney 518:16	350:16 351:1,9
454:6 479:4	associated 17:15	484:3,17	attributable	351:12,17
515:10	20:3 80:2	491:12 494:6	191:17 199:13	358:9,16
asking 16:4	158:3 175:20	498:16 505:24	241:24	359:16 360:13
24:10,14 27:16	176:7 182:8	506:2,4 507:18	attributed 444:8	362:7,20
97:10 141:6	189:19 243:24	assumed 408:24	author 6:16	367:14 374:1
152:18 167:13	245:6,16	assuming 35:2	121:21,23	376:21 379:9
167:21 168:1	265:11 266:4	226:19 297:13	122:2 152:19	379:15 394:2
168:10 184:15	301:15 454:18	319:18 323:20	184:9,18 194:1	395:13 397:12
195:14 196:3	association 6:22	326:20 369:1	194:22 211:17	397:21 401:5
208:11 212:11	7:12 87:18	423:19,20	249:4 257:5,18	401:23 402:23
292:11 297:17	124:9 149:23	433:15 444:1	264:2 287:3,6	411:13,16,22
332:16 348:19	150:4,8 164:8	491:23	287:9,12 300:2	412:10 413:18
370:21 371:24	165:2 202:16	assumption	399:4 445:8	414:5 417:8
372:3 385:10	203:23 220:23	178:1,3 265:13	author's 211:14	418:8 423:10
422:10 440:16	229:6 246:14	279:1 331:24	authored 468:23	424:5,7 427:14
458:11,15	246:19 247:16	337:6 369:11	authoritative	428:18 430:7
480:10 483:6	249:21 259:9	436:23 479:12	195:14	431:17,24
483:11,14,24	259:12 260:11	480:9 481:5,10	authority	435:24 436:7
485:12 500:11	260:18 262:15	481:20 485:1	194:13,18	436:11,18
asks 482:13	265:15 268:20	assumptions	195:4,19 196:5	437:13 439:19
511:16	272:3 307:23	107:24 108:7	199:11 219:8	439:19 441:4
aspect 429:22	310:6 312:22	108:11 332:1	219:13,16	443:2,6,9,13
aspects 430:9,15	313:9 351:4	341:2	372:17 373:1	444:18 445:3,4
aspirin 452:19	357:16 374:15	atomic 326:14	authors 89:1	445:14,17,19
453:23 454:12	375:10 378:10	331:22 335:17	121:24 123:4	446:23 454:16
454:17 455:11	408:23 409:11	336:11 353:5	147:24 178:15	487:18 488:5
455:15 456:3,9	420:16 429:11	attached 51:16	184:24 190:19	492:10
456:15 457:10	432:8 433:21	52:24 57:12	201:3,6 203:12	authors' 476:21
459:6,17	443:5 444:19	105:6 117:4	210:17 212:16	available 220:20
461:17	445:6 446:16	518:12 520:11	212:21 214:15	224:18 325:18
assess 391:19	453:22 454:1	attempt 48:22	215:1,17	419:13 420:18
assessed 509:16	476:15 484:10	122:9 123:5	217:11 218:3	504:5

Avenue 1:14 11:9 average 405:7 avoid 15:18 aware 28:6 30:7 30:14 31:15,20 32:2,8 42:23 79:9 94:1,4 144:23 154:17 229:19 243:22 244:20 245:1,3 247:6 253:10 253:16 267:2 288:12,14 306:19,23 333:12 390:19 391:1 419:2,11 437:23 438:18 440:5 491:2,8 491:10 495:19 496:1,2,10 501:18 510:8 512:16	397:6 400:24 421:20 428:14 431:5 435:19 446:11 453:13 461:4,9 473:23 476:8 477:23 486:6 489:16 510:12 baked 283:22 balance 229:13 bank 395:20,21 bar 445:20 base 442:6,12 based 7:19 18:14 43:12 44:9,16 48:18 61:16 62:10,11 71:24 76:5 87:20 150:15 156:1 164:23 179:1 185:13 188:2,13 204:21 219:7 244:22 252:5 252:10 260:8 264:24 268:11 282:2 289:4 329:11 333:10 335:23 341:3 341:21 373:14 375:17 402:12 403:1 439:5 442:8 447:24 464:19 494:2 509:14 511:18 513:23 514:3 baseline 78:16 376:5 bases 37:17 basic 57:1,5,16 58:5 59:1 153:12 205:11 461:2 basically 225:11 227:8,8 231:10 322:8 475:10 basing 52:3	508:21,22 511:7 basis 47:24 123:15 124:8 285:12 322:14 336:15,16 357:20 362:6 433:11 447:18 447:22 464:16 Beach 2:4 bear 75:8 BEASLEY 2:12 becoming 264:16 began 38:4 41:14 351:19 352:10 368:21 beginning 1:15 59:10,21 97:7 116:12 270:4 307:10 308:5 379:2 380:12 begins 201:17 256:8 275:18 378:8 469:7 behavior 340:10 behaviors 252:4 belief 449:10 beliefs 284:7 believe 14:2 28:20 36:4 37:5 38:3 43:5 43:24 49:7 51:21 54:8 55:11 62:19 64:24 65:5,8 67:22,24 69:7 70:3 92:2 99:14,14,24 121:16 127:17 135:23 138:1 151:1 157:19 157:21 163:2 174:17,19 177:2,21 180:2 187:24 188:24 212:13 213:24	221:14,17 243:10 245:5 245:10,20 248:18 252:7 261:14 267:15 267:19,22 268:2,3 271:2 282:1 285:17 295:5 308:7,10 362:22 369:17 369:21,22 372:7 373:11 409:4 410:23 411:4 413:6 414:9 436:19 437:11 447:9 451:15,23 454:20,23 455:17 456:13 458:23 470:9 487:4 501:11 believes 340:24 believing 179:15 bench 153:22,24 benefit 33:16,19 34:10,15,22 35:12,24 36:6 36:16 37:6 benefiting 35:6 benefits 33:4,12 benign 487:11 Berge 9:14 229:23,24 231:20 233:9 234:5 236:7 237:1,6 238:4 238:4 259:11 261:21 290:12 290:17 314:5 318:11 319:3 319:12 320:20 320:24 321:8 322:5,7,13,15 322:22,22,22 328:23 329:9 329:19,21 408:11 409:6	409:23 471:12 472:19 Berge's 227:8 230:16 best 130:5 196:17 197:2 197:18 282:6 302:23 488:20 489:5,22 490:5 bet 264:7,9 better 197:15 388:21 413:7 512:9 Beware 204:7 210:9 bias 137:18 196:11 198:21 198:21 199:1 199:14 226:5,6 226:10 252:11 252:16,21 253:20 254:7 254:22 256:14 256:20 257:3,8 258:3 259:6,7 259:14,15,20 260:3,5,14 261:5 262:1 263:10,21 264:19 267:1,6 268:10 271:24 272:9,13,15,16 272:21 273:8 274:5,11,24 276:11 277:1,7 277:10,12,22 278:11 280:12 290:22 291:2 291:19 292:1,9 307:14 314:18 361:9 biased 189:10 290:20 291:17 291:24 biases 205:4 bibliography 152:14
---	--	--	--	---

BIDDLE 3:7	450:13	430:9,16	398:1	428:15,19
big 264:6 300:5	bodies 423:4	431:15 436:6	buried 148:14	430:7 431:16
389:11 436:22	body 7:12 29:14	477:18	business 281:19	436:7 439:20
biggest 122:18	43:13,16 57:9	branch 494:9	305:20	446:11 477:16
236:23 238:24	67:9 120:8	BRCA 455:22	businesses	Canada's
bill 112:24	133:2,5,21,24	break 25:7	495:21	142:13 143:12
biologic 116:6	134:2 136:24	73:11 125:10	Buz'Zard	419:17
126:21 162:15	206:16,20	125:19,24	139:13 162:16	cancer 6:13,23
164:18 165:9	210:19 231:17	126:3,5,13	163:19 165:24	7:7,10,13,14
165:22 296:13	235:4 272:4	223:23 239:17	166:5 167:2	7:22 8:7,10,13
308:2 340:1	276:10,14	285:1 343:16		8:15,17,21
391:16 394:22	289:11 312:8	343:20 348:19	C	9:14,16,18
395:8 401:2	389:12 390:11	421:14,18	C 5:23	13:3,11 14:15
403:8 430:14	483:1,15,21	485:20 486:4	CA-125 434:7	17:5,9,11,17
431:14 432:7	498:3 509:6	breaking 125:15	434:17	18:19,22,24
437:7 460:14	bomb 326:14	239:11	CALCAGNIE	19:6,18,22,23
477:19	331:22 335:17	breast 244:6,12	2:3	20:2 21:4,16
biological	336:11 353:5	244:21	California 2:4,9	21:17,20,20,22
164:13	Bonovas 453:14	Brief 348:13	7:8 226:11	22:8,13 23:2,4
biologically	book 100:18	453:11 473:12	call 40:3 49:8	23:10,21 24:23
140:6 174:1,13	101:6 287:19	briefings 37:19	123:19 150:10	25:3,4,8,24
393:5 394:6	Boston 3:4	bring 26:7	158:14 184:19	28:2,9,19,22
401:6,24 422:1	226:8	120:22 314:14	201:10 214:16	30:9,16 31:16
422:19 423:12	bother 194:10	363:5	242:22 392:18	32:4,13 37:23
427:16 436:12	219:21 315:9	bringing 118:23	426:4 458:7	44:4,16,23
437:12 439:21	bothered 392:7	broad 64:2	470:22 498:10	46:13 56:24
440:7 441:5,20	bottle 100:15,17	101:13 139:7	called 151:23	60:15 61:14,20
492:17	101:9 102:2,3	broader 191:6	273:19 299:23	61:23 62:16,23
biologist 153:7	500:20 501:4	Broadway 2:8	calling 298:20	63:14,19 65:2
153:13	bottom 181:10	broke 409:8	427:8 490:5	65:6,10 67:23
biomarker	181:11,16,21	broken 387:18	calls 387:13	68:2 69:13
151:20	200:8 210:8	brought 87:4	camera 211:19	70:1,11,20
Birrer's 135:22	334:21 358:2	103:15 294:23	348:9	71:2 77:15,24
140:15,17	429:24 430:4	304:1 495:4	Campus 3:8	78:2,22 79:19
bit 42:14 61:6	486:21 497:2	BROWN 2:8	Canada 143:20	79:20 86:23
87:3 88:1	Boulevard 3:4	468:12,14	143:23 144:4	87:19 88:24
240:23 336:1	bound 16:2	brushing 250:20	144:13,20	89:4,6 90:2,4,8
445:20	box 244:21	Bucketing	145:24 171:10	90:9,14,21
black 244:20	319:13	215:19	171:21 220:3,6	91:7 93:11
Blair 156:18	boy 487:2	built 283:21	220:11 222:21	95:11,16 97:9
157:5 292:4	Bradford	bumped 491:22	258:21 261:4	97:24 98:18
blocking 445:10	115:20 160:5	492:5	324:24 325:9	100:5 101:7,17
BLOOD 2:7	161:14 164:5	bumpers 196:14	329:5 331:7	113:18 116:10
blue 186:18	233:19 246:5	196:14 205:20	402:15,18	120:7,8,9,14
187:1,2,3	247:11 427:15	bunch 221:14	403:7,11 414:1	120:15 124:10
189:21 270:1	428:21 429:4	226:4	414:2 419:3	138:2 145:8,15
board 448:22	429:11,15	burden 396:7,11	420:4,7 427:13	149:9 151:12

151:19,22	378:14,18	17:4 19:14	carefully 93:8	238:12 240:2,8
153:5,7 165:3	380:4 385:13	20:1,7,8,10,14	518:4	241:4,11,16
165:23 174:16	386:1,4 394:5	21:7,10,13	caring 243:15	252:8,15,21
174:20,23	396:20 405:9	96:11,17 97:1	carried 306:22	257:7 268:11
175:7,16,20	405:12,16	97:5,8,12,13	366:21	272:1,23 274:6
176:8 180:12	408:6 409:21	97:21,23 98:7	carries 15:9	274:12 275:1
182:2,9 189:19	410:19,20	98:21 99:9,16	244:20	282:9,20 283:4
205:17 206:8	413:12 419:6	99:20 101:16	carry 207:21	290:8,15
206:12 221:1	419:19 420:16	101:19 102:2,4	332:10,10	293:24 294:5
224:21 241:6	421:9 432:12	228:5 326:9,19	cascade 432:11	294:12 295:12
243:11,24	432:20 433:12	335:16 336:24	case 14:10 38:2	298:18 304:24
244:4,7,12,21	433:18 434:6	396:15,16,24	39:4 40:23	306:21 307:15
245:6,16	443:24 444:21	420:2 421:5,8	44:14 45:22	307:21 308:8
246:15,20	446:18 447:13	421:12 491:14	46:8 47:16,20	308:16 309:16
248:12 249:19	447:24 448:2	492:22 501:13	48:1 49:22	309:23 310:4
252:10,17	449:9 450:5,14	510:24	50:8 60:12	311:15,17
253:19 254:6,8	451:10,14	carcinogenesis	94:3 110:2,3	312:19 313:1,4
256:16,23	452:16,20	57:6 425:15	113:13 152:6	313:5,11 314:4
262:23 265:12	453:17,23	carcinogenic	152:16 154:6	315:13 319:1
266:17 267:5	454:2,13,19	17:7 74:23	162:18,22	324:4 325:1
272:4,17	455:5,14 456:1	75:15 76:2	181:13 182:3	329:4 381:10
276:15 278:14	456:8,16 460:1	85:16 109:14	227:1 228:19	453:19 506:11
280:17 306:20	461:23 464:19	369:13 451:1	292:6 305:9	cases 1:8 13:11
310:2,21	465:3,7 466:5	carcinogenicity	307:5 313:18	44:10 52:4
311:12,23	466:13 467:9	22:4 57:17	324:1 332:23	53:14 56:23
312:1 316:5	468:21 470:8	58:6 89:19	339:7 346:11	58:20 93:9,17
317:9,10	476:16 479:15	90:1 95:2	366:16 386:14	93:19,24 94:1
324:11 325:13	479:23 480:17	140:7 142:9	398:11 434:10	94:5 247:3
325:18 326:5,6	481:24 482:6	249:5 393:6	448:12 449:1	263:4,6 264:15
326:7,11,13,16	484:15 487:2,7	394:21 419:15	491:15 497:22	266:19 280:5
327:1,10 331:8	487:21 488:17	439:6 491:4	512:15 515:5	317:23 325:15
331:17,18	501:3 505:21	carcinogens	case-control	391:2 392:1
332:23 334:11	507:20 508:11	59:2,2 71:12	100:24 115:18	397:1 450:5
334:23 336:4	508:11 510:15	96:7	137:8 148:22	catch 28:14
336:19,23	512:13 515:9	carcinoma	149:11,15,21	385:1
337:4,15,17	cancers 26:10	152:2 311:1	150:6,14 182:5	categorical
338:16 340:1	43:14 378:20	448:20 449:14	182:23 183:12	216:3
342:4 347:5	452:7	476:17	183:23 187:19	categorically
351:5 353:17	capable 209:5	carcinomas	188:1,12 189:1	215:23
354:17,23,24	capacity 145:7	461:13	191:9,20	categorization
355:7,10,11	151:16	care 9:9 13:14	192:16 193:1	217:12
356:19 357:10	capture 325:15	77:19 243:18	198:18 206:22	Categorizing
357:18 358:1	captured 344:11	288:20 289:4	219:5 222:4,6	215:16
363:2 367:7,8	344:16 389:4	396:21 450:15	222:17 226:7	causal 18:18,20
367:16 369:2,5	capturing 388:4	514:4	231:23 233:11	46:11 87:18
370:7 372:11	carbon 135:23	career 28:19	234:12 235:2,4	393:23 419:5
374:17 378:12	carcinogen 17:3	careful 67:5	237:3,13	419:19 420:18

421:2 436:8 causality 157:11 410:12 causation 6:11 44:9 108:17 110:15 155:23 165:10 171:8 171:19,21 172:6 499:7 causative 421:8 cause 17:8 28:9 44:15,23 60:14 61:14,23 62:16 62:23 63:18 65:1,6 67:23 68:2 95:11 97:9,24 101:7 116:10 174:18 175:6,12,15 210:13 224:21 276:24 337:4 339:24 432:12 432:19 433:11 434:5 447:20 447:24 465:7 504:12 507:20 508:11 510:15 512:13 caused 18:21,23 19:5 277:10 396:20 461:24 causes 17:5 20:4 28:18,21 43:14 44:4 77:15,24 78:1 138:2 174:20 205:17 277:6 331:16 336:23 337:15 433:18 448:17 479:22 480:16 481:24 482:6 505:20 causing 331:18 431:19 caution 321:2 caveat 373:4 cavity 423:5	425:17 CEBMA 281:15 cell 19:12 152:2 250:2 260:22 261:1 409:6 cells 19:11 433:18 460:19 cement 63:8 69:10 Center 12:18 281:14 301:3 427:3 428:11 Central 7:7 certain 9:20 28:1,1 77:13 101:23 106:18 251:18,19 259:23 262:13 266:19 284:6 394:20 456:7 496:3 497:9 502:10 504:2 certainly 412:7 certainty 17:24 18:10,14 372:5 CERTIFICA... 517:2 certification 517:18 Certified 1:16 1:16 517:13,14 certify 517:5 520:5 certifying 517:22 cervical 120:14 120:15 cervix 205:17 cgarber@robi... 2:5 challenged 266:23 chamber 260:9 chance 27:18 150:11 188:21 191:17 193:21 199:13 228:18	242:1 290:14 326:15 329:2 354:13 409:17 change 175:3 253:7 255:10 293:11 368:9 417:11 433:17 492:23 494:8 497:22 499:7 499:13 510:16 511:9 513:18 519:4 changed 412:11 514:3 changes 252:4 293:9 511:19 518:11 520:10 changing 371:11 characterizing 168:12 check 309:13 384:15 chemical 151:23 chemotherapies 320:11 chemotherapy 320:8,9 Cheryl 147:2,18 Chicago 4:4 child 399:8 choose 361:22 chromium 109:6 chronic 174:14 174:18 448:8 451:4 chronological 270:7 churning 236:4 cigarettes 342:15,15 circle 258:14 circumstances 303:2 citation 138:12 285:16 286:3 303:3 333:19	335:14 337:8 citations 129:17 335:21 cite 76:6 98:16 132:4 229:19 261:12,13,15 261:16,17,20 275:3,10 276:18 285:19 290:24 356:16 372:16 379:17 380:4 381:23 383:6 432:2,14 437:8 438:9 443:22 460:7 cited 45:19 61:17 62:8 93:14 180:3 199:10 285:23 331:3 333:20 352:2 382:4 418:19 458:21 459:1,21,23 cites 248:24 259:8,11 378:13,14,24 382:20 444:17 446:18 citing 185:12,13 263:17 379:10 381:3 437:14 488:5 claim 136:22 150:13 194:14 194:19 199:16 201:10,19 204:1 268:18 336:17 claims 199:11 217:13 Claire 495:22 Claire's 9:20 496:5 497:10 497:17 498:9 clarification 24:14 59:14 clarify 16:5	23:17 33:18 46:20 47:11,15 52:13 54:2,3 100:1 152:17 166:21,24 190:1,14 191:5 385:10 465:13 490:3 clarifying 99:3 191:4 Clarke-Pearson 156:17 157:4 Clarke-Pears... 137:20 class 275:12 276:8 286:14 classification 493:11 510:22 classify 94:11 clean 29:1 clear 15:23 16:10 51:24 69:7 88:11 152:2 180:24 202:13 264:10 294:18 357:3 409:6 421:23 428:4 458:19 515:4 clearly 78:3 87:20 95:8 100:3,6 127:15 147:13,17 204:23 358:3 379:24 457:18 clinical 86:7 205:13 275:2 288:19 289:4 302:24 304:2 305:9 330:16 335:3 448:13 453:20 clinician 242:12 clinicians 67:5 295:11 close 125:13 318:19 474:22
---	--	--	---	--

closer 73:19 356:7	356:11 357:15 361:15 373:10	264:10 265:24 266:23 297:10	134:4	208:22 210:18
closest 324:19	378:10,21	308:12 321:14	comparison 101:5	210:23 211:2,8
closing 100:17	405:21 406:4	360:19 410:7	comparisons 320:6	212:22 213:1,8
CMO 30:24 31:2	453:21 479:18 506:12	410:15 419:19	compatible 217:18	249:5 295:10
co-author 152:19	cohorts 241:4 282:8 283:4	comes 196:7 229:1 426:13	compel 502:18	314:2,3,8,21
co-carcinogen 342:19	298:17 304:24 305:9 311:18	coming 27:19,22 94:19 108:16	compelled 500:8 501:4	356:8 480:12
coached 209:15	313:16,18	161:5 172:15	compelling 484:13 505:20	480:13,15
coaching 208:9 208:11 209:2,6	315:11 316:11 363:11 364:21	179:14 227:4 228:23 320:1	compensation 107:12 114:15	513:10
209:12,14	366:4 401:1	399:12,17	complete 26:5	concerning 103:18 145:7
cobalt 109:6	406:8,13	403:2 419:4,14	45:19 103:16	concerns 61:2,3
Cochrane 304:5	coin 310:8	493:13	354:9	313:20 411:10
code 79:11,13 79:14	collaborate 153:19	comment 143:19,23	completed 51:7	conclude 90:16
cognitive 215:18	collect 388:9,10 388:13	144:2,12,21 200:22	completely 209:4 458:18	202:14 203:21
cohort 48:2 87:21 100:9	collected 256:19	commentary 81:4	completeness' 352:12,23	217:11 362:7
115:18 137:14	collecting 194:24	commenters 226:15	completion 517:8	424:6,8 436:7
137:22 149:12	collective 419:4 504:7	comments 67:2 214:7,11	comply 103:12	441:5
170:14,22	color 186:14,18 490:13	Commerce 2:14	comprehensive 90:19 91:23	concluded 222:21 237:21
182:6 206:22	color-coded 187:14 269:23	commercial 264:8	92:19,23	253:19 254:6
206:24 207:8	column 87:13 181:22,23	commission 520:21	131:16 132:2	423:11 427:15
222:4,10,15	182:20 214:15	common 66:23 204:4 294:14	149:3 224:17	435:19 439:21
237:3 238:11	217:10 256:7	455:21 500:5	233:15 514:23	447:2 477:17
238:15 257:7	271:18 275:16	commonly 260:15 294:19	comprises 378:19	492:20 516:7
282:19 290:6	293:4 334:19	community 217:21	computer 106:18 107:2,5	concludes 491:13
290:17 291:1	351:1,13 377:5 377:21 486:20	company 154:12 154:21 478:16	107:8 187:11	concluding 223:1
293:23 294:4	combination 243:1	478:21	concentration 435:16,18	conclusion 88:5
294:11 295:12	combine 222:3 222:12	compare 320:10 474:16	concept 214:17 339:13 389:13	88:5,22 89:7
307:4,12 308:1	come 26:10 47:12 55:17	compared 197:20 254:18	concepts 293:10	94:8 127:15
308:9,15,22	88:21 89:6	262:23 444:12	concern 14:13 151:11 152:5	128:21,22
310:14,19	94:7 95:18	comparing	153:3,4 272:7	205:9 222:5
311:2,15	189:17 195:24		469:9 504:12	224:11 227:4,5
313:21 314:15	222:5 229:4,12		505:9,10,13	228:4 229:2,5
314:17 315:4			concerned 69:12	419:18 435:23
315:24 316:1				493:14
316:15,18				conclusions 67:3
317:8,14,23				74:22 75:13,24
324:4,9 325:2				76:5,8 77:11
325:16 329:2				85:15 91:10
329:16 330:1				210:9 211:14
331:9 336:8				conclusions' 204:7
345:23 355:6				conditions 289:17 438:22
				487:12

condoms 236:19	401:18 445:18	272:8	497:9	508:14 515:7
conduct 26:22	conjunction	consist 104:4,6	Cont'd 3:1 4:1	continues 168:3
119:21 145:13	449:15	157:1	6:2 7:2 8:2 9:2	503:24
153:15 284:24	connection	consisted 46:24	contact 84:6	contradictory
293:10,13	13:14 14:18	consistency	411:12	184:4 185:18
439:7	58:17 59:11	94:20 116:5	contain 96:10,11	210:12
conducted 22:2	106:7,14	137:11 158:8	96:23,24 97:13	contrary 128:4
91:22 126:20	113:15,17	158:20 164:9	98:6,7 109:5	132:24 171:8
379:4 380:2	116:16 129:21	182:22 184:8	109:14 175:2	171:18
431:16 499:4	243:16 440:2	184:15 205:6	479:3 480:24	contrast 204:2
conducting	consensus	220:6 224:10	482:12,16	Contravening
145:5	173:10	225:12,21	483:23 485:2	93:13
conference	consent 338:14	226:1,2 233:20	504:15 505:4	contribute
15:12	340:8 352:18	410:11 429:14	contained	61:20
confidence	352:20	consistent 68:17	109:23 115:15	contributed
149:24 187:5	Consequently	149:18,19	157:6 177:15	93:12
189:4 193:23	469:15	150:11 165:1	228:1 241:6	contributors
194:8 196:13	consider 24:6	182:24 183:2,7	353:8 492:19	205:10
196:23 197:14	97:19 98:20	183:13,23	containing	control 305:10
202:5,21	131:5 149:18	184:5,11,20	75:17 84:24	346:13,14
205:20 219:8	149:18 153:6	185:1,24	85:20,22	517:21
235:23 347:16	153:11 158:8	206:21 220:22	contains 97:11	controlled 285:4
348:23 353:18	189:11,12	221:18 222:22	102:4 148:3,18	controls 262:24
354:18 370:8	193:19 194:5	223:9,12	512:20	263:1 280:4
372:8 376:24	195:2 233:12	224:14 225:2,7	contaminated	324:2 435:15
378:16 386:5	272:16 279:23	225:17 227:12	498:15 506:14	controversial
386:10,12	307:2 336:22	227:13 233:19	contamination	284:20 285:14
387:2 474:21	352:5 370:24	260:22 272:10	122:10,20	convention
477:10	379:13 434:8	273:16,19	123:6,20	294:24
confidential	considerably	284:14 310:4,7	398:19 399:10	conversation
154:23	495:16	336:7 410:20	399:13,23	66:14 400:20
confirm 45:3	consideration	417:10 420:13	400:5,7 498:12	483:19 501:19
404:9	376:18	420:14 446:4	504:2 505:14	501:21
confirmation	considered 37:3	452:24	505:19 506:7	conversations
78:15 94:7,14	93:8,24 98:22	consistently	contend 126:24	502:4
confirms 449:10	98:24 107:21	149:7,17 158:2	content 154:15	convince 338:20
conflict 203:2	128:3 137:17	158:4 470:10	contention	481:23
confounder	155:12,19	consists 104:11	412:9	convinced 94:16
196:10	195:10 219:14	104:22	context 17:11	123:1 440:20
confounders	271:24 304:8	constant 169:7	18:19 19:4,17	convincing
205:3	304:11 323:4	constantly 48:23	19:21 27:12	99:11 482:5
confused 24:4	355:24 381:18	constitutes	34:4,23 35:13	492:4
82:22 365:2	419:3,12	195:18	59:4 286:22	copies 105:17,22
415:4	463:23	consulting 41:15	298:8 428:21	106:1,4 255:24
confusing 84:19	considering	42:22	429:4 430:9	408:2
conjecture	494:24	Consumer 84:2	continue 469:8	copy 39:24
398:13 400:10	considers 272:6	consumers 9:19	504:6 507:20	71:14,17,21

73:13 103:16	193:10 203:12	182:10,11	232:19 315:9	criticizing
148:9 151:2	204:17 206:8,9	183:19 184:3	315:12 372:10	312:18,20,23
186:14 417:17	206:11 216:5	201:23,24	458:7 518:20	313:11
417:18	219:1,9 225:6	203:7,10 204:8	cover 159:5	critique 172:13
Cornell 7:18	235:20 249:15	212:10 215:12	coverage 266:9	critiques 61:1
12:17 242:10	259:23 261:10	217:7 224:23	covered 372:16	173:2,7
301:2,20 302:5	265:1 275:4	224:24 259:17	covering 356:7	cross 187:5
302:16 448:21	281:11,16	272:11 276:16	COX 459:24	194:9 474:22
461:4	286:23,24	289:24 297:3	460:18,19	cross-examina...
Cornell's 301:24	287:15 289:12	297:18 302:19	461:16 462:2,2	298:9
corners 161:3	296:19 305:11	322:23 351:7,8	COX-1 461:14	cross-trial 320:5
161:10 273:6	309:16 317:17	378:22,23	COX-2 461:14	crosses 189:4
273:13 356:17	317:20 333:9	420:20 431:21	Cramer 122:1	386:18,20
357:8 405:23	333:15 344:18	432:15,16	123:19,20	crossing 354:4
406:11	345:5,10 346:4	444:22 469:19	135:1 232:3,4	crucial 201:11
cornstarch	347:11,12,17	469:20 487:16	232:6,6 265:16	crude 264:14
514:8,19,24	349:1,4 350:2	504:10	338:24 340:23	cry 346:2
corollary 102:3	351:10,15	correlation	369:22 398:15	culture 19:12
434:17	353:19 355:1	132:6,17	398:16 399:5	cumulative
Corporate 2:4	360:14 363:24	391:22 397:6	399:12,13	344:17
correct 13:7,8	364:1,12	cosmetic 9:20	crazy 232:20	cure 73:10
18:10 20:17	367:11 368:3,4	33:1 84:3	create 148:24	curious 208:2
22:17,21 29:19	368:17,18,21	495:22 496:4	187:9	229:15 267:16
40:23,24 41:3	368:23 370:13	497:10 504:3	created 22:23	297:1 335:13
42:2 44:11,12	372:19 374:2	counsel 25:13,23	23:3,20 150:12	461:7
47:20 48:6	375:19 379:11	44:18 47:1	407:23	current 25:2
60:15 74:7,14	379:12 382:17	48:13 116:20	credible 176:3	currently
75:19 82:9	389:9,10 391:6	117:6,13 298:9	177:17 495:12	210:10 224:18
84:13 86:1	394:7 395:14	354:13 462:13	credit 28:18	439:15 491:3
89:20 95:3	401:8 402:5	478:9	Crest 250:21,24	515:12
105:7,8 106:2	403:13 404:2,8	count 233:10	criteria 160:6	Curry 3:3 16:23
111:23 112:8	405:24 406:13	counted 264:8	164:5 247:12	17:12 18:1,11
114:6,7,9,10	410:20 411:19	381:11	420:14 428:21	19:1,19 20:19
114:13 115:3,4	411:24 413:20	counting 399:15	429:5,11,15	24:1 25:15
115:7,8 116:17	426:10 432:3	countries	430:10	26:2,23 27:3
118:7 119:4,9	433:23 436:15	240:14,18	critical 9:9	27:13 28:3
124:21 125:6	438:17 440:9	counts 397:7,14	130:18,23	29:2,20 32:17
134:10,13	443:16 447:3	couple 55:21	criticism 162:9	33:7,13 34:17
140:2 142:15	451:4 465:2	88:18 130:10	312:13	34:24 35:15
143:2 146:4,17	470:14 472:23	315:23 336:1	criticisms	36:1 38:22
146:18 148:3	473:20 474:9	444:7 460:8	136:21,24	39:5,23 42:3
166:1 170:10	488:6,21,24	course 29:16	156:23 157:5	43:22 44:19
170:11 171:22	489:1,6 520:7	251:7 284:10	314:14,15	46:2 47:2 48:7
172:16 173:3	corrections	284:13 354:3	315:2 355:21	49:17 50:14
174:9 176:19	518:5,7 520:10	438:5	361:19 411:8	51:2,19 52:12
176:24 186:11	correctly 76:11	court 1:1 11:16	criticize 312:14	52:15,19 53:4
186:12,20,23	76:13 84:9	15:11,16 209:9	458:13	54:2,3,18

55:22 56:11	183:6 185:2	318:5 319:8	464:10,20	62:11 64:4,7,8
57:19 58:8	188:4 190:22	327:12 328:1	466:22 468:8	70:17 72:13
60:5,16 61:24	192:3,17	330:7 331:11	469:2 470:15	74:16 106:15
62:17,24 63:21	193:12 195:5	333:1 335:7	472:8,15	106:17 107:19
65:16,21,23	196:18 197:4	338:6 340:20	475:23 477:20	115:17,22
66:4 68:5 70:3	198:13 202:7	341:4,8 342:10	480:5 481:2	137:7 149:7
70:12 72:19	202:22 203:13	343:8,12	482:18 484:19	164:16 171:8
74:1 77:4 79:6	204:12 207:1	344:19 345:11	485:4,23	171:19 177:3
80:20 81:15	207:12 209:4	346:5,16 349:5	487:22 489:9	177:14 178:15
84:14 89:21	211:5 213:5	349:20 350:19	491:5,17	178:17,19
90:22 91:24	215:3,9 216:6	354:9 355:12	492:24 494:11	179:3 184:11
92:10 95:4,20	218:4 219:10	356:20 358:11	496:7,16	184:19 185:1
96:12 98:8	221:6,21 223:4	359:1,10	497:23 499:8	185:23 187:13
99:21 101:20	223:21 225:3	360:16 362:10	500:2,13,21	188:1,12 189:9
102:7 103:6,19	230:10 231:4	364:5,13,23	501:8 504:16	194:24 197:10
104:13,23	232:15,22	365:8 366:6	505:6 506:21	202:4 216:3
106:8 107:15	234:16 235:7	369:7 370:18	507:23 508:16	219:5 220:7
108:12 109:7	235:13 237:15	372:20 375:20	509:23 510:18	224:19 225:2
109:15 112:15	237:24 238:20	377:6,11 378:1	512:3,22	225:14,19
113:22 116:21	239:10 241:13	379:20 381:7	513:12 514:10	227:3,6,9,10
117:7,23	242:2,13 244:1	382:23 385:6	514:16 515:23	228:24 229:9
118:18 119:5	244:14 245:8	385:19 386:6	curve 339:18	230:23 231:2
121:9 122:6,16	245:22 246:7	387:5,15 388:6	custom 25:23	235:6 236:5
124:11,23	246:22 248:3	388:14 391:7	cut 136:3 138:24	256:19 260:8
125:9,16 127:9	249:7,22	393:7 394:8,14	148:10 166:23	263:17 268:17
127:20 130:20	250:11 251:14	395:15 397:15	212:8	273:16,17
131:20,23	252:12 253:2	398:3,23	cutting 163:13	276:11 277:21
133:11 136:13	253:21 254:9	399:19 400:3	167:24	288:20 296:18
137:2 138:23	257:12,21	401:9 402:2,10	CV 22:6 150:22	314:1 324:22
139:6,23	259:24 262:8	406:1 408:1,17	152:13,22,23	330:15 336:7
141:15 142:3	265:5 267:8	410:21 412:13	153:17	337:16,18,20
142:16 143:3	268:13 272:24	412:21 413:21	cycle 438:1	339:21 358:17
146:6 147:5,11	276:2 277:18	414:19 417:16	CYNTHIA 2:3	362:4,8 366:20
148:8 150:17	278:16 279:2	419:8,21		370:1 373:15
152:7 153:8	282:11 283:13	423:17 427:19	D	379:18 384:9
155:2 156:3,14	286:16 287:24	431:8 432:21	D 5:2 488:23	386:5 390:20
157:17 159:1	288:9,23	433:6 434:1,19	D.C 3:18	392:9,15 393:3
160:20 161:7	289:21 291:4	435:6 436:16	daily 248:21	398:18 403:1
161:24 162:19	295:15 296:2	438:2 439:9	250:5 251:9,11	417:3,10
162:24 163:12	296:20 298:24	440:11 441:11	345:4	420:18,23
165:11 166:2,9	300:18 302:1	441:24 442:10	dangerous	423:8,23,24
166:12 167:15	303:12 304:14	447:4 448:3	501:13	436:8 438:13
170:16 171:12	305:16,22	451:5 452:21	data 21:8 30:7	438:18 440:6
172:1,7,17	306:16 307:7	454:21 457:2,5	30:14 31:15	440:23 441:23
173:4,14 174:4	312:2,15	459:10 460:3	32:3,6,9,20	442:9,17 448:1
175:21 176:4,9	315:15 316:6	462:5,16,21	46:7,22 48:19	450:19 452:11
177:4,18 179:5	316:22 317:18	463:6,14 464:5	49:5 57:18	452:19 455:10

455:13,15,18	169:9,12	defendants 3:15	deposition 1:13	268:5 280:1
456:7 457:10	487:19 518:16	154:6	6:6 10:2 11:8	283:21 307:14
458:21,24	Dcurry@nutt...	defending 209:5	13:5,10 15:3	308:24 309:1
459:8,8,22	3:5	defense 238:19	37:16 40:22	309:12,15,19
460:2,7,12,22	deadliest 455:20	define 17:19	45:10,13 48:14	312:19,24
464:19 470:5	deadly 206:11	18:18 21:6	54:6,14,19,23	313:12,15,17
474:2 481:21	206:14	198:11 470:24	55:3,6 56:21	315:10 316:18
484:6,16,22,24	dealing 84:22	defined 7:20	58:18 59:8,16	319:21,24
485:11,13,17	deals 151:18	68:21 193:18	59:20 60:3,22	323:3,5 329:15
488:6 491:12	debulking 78:20	302:18 384:8	61:7 64:17,19	338:1 340:12
491:20,24	debunk 295:6	472:21 474:10	65:18 102:12	388:23 410:7
492:4,11,13,16	295:13 296:16	defining 48:16	102:18 111:11	410:15
492:16,17,18	decades 240:9	definitely	111:22 113:2,3	designated
493:19,21	339:2	129:13	113:6 114:17	37:10
498:14 502:5	December 6:20	definition 19:16	147:7,18 284:6	designations
508:20,23	142:15 143:12	80:4 97:8,13	461:1 496:14	210:13
509:15 511:11	220:12	97:23 98:13	516:4,7 517:6	designed 308:12
511:11,18	decide 144:5	177:7 184:7,15	517:8,9 518:3	308:15,16,17
512:8 513:8,15	236:14 264:2	195:10,15	518:13,17,19	316:2,12
513:15,18,21	278:19 509:8	197:22 198:1,2	depositions	319:19 338:13
513:21 514:4	decided 323:19	198:5 302:21	15:15 54:7	479:13,16
514:24	decision 508:19	347:19 370:12	111:5 119:19	designer 337:13
dataset 150:4	decisions 203:6	371:12 427:10	121:3 124:1	designs 241:7,12
232:2 233:15	288:19 289:4	definitions	deps@golkow...	286:1 293:21
date 1:15 11:6	declarations	16:10 18:7	1:21	308:11 321:6
114:6 180:13	217:14	362:14	deputy 428:10	331:10
182:23 183:13	decrease 187:8	definitive	dermal 84:6	desirability
264:6,15	457:11	205:23	describe 115:13	252:1
266:12 379:3	decreased	degree 17:23	128:2 173:7	detailed 420:12
380:1,6 491:13	452:20 455:14	18:9,14 62:3	183:24 194:23	detect 317:11
503:10 518:9	459:8	116:1 164:19	214:19 392:17	318:1,21
520:16	decreases	179:18 272:20	396:6 402:17	325:20 328:21
dated 49:14	456:16	372:5	described 63:5	329:17 330:4
104:12 142:14	deduce 63:12	degrees 154:3	222:9 247:15	330:19 338:4
220:11 424:16	deem 152:5,15	Demonstrative	263:22	351:3 369:4
486:11 517:15	177:15	8:20	describing	detection 151:18
Daubert 6:11	deemed 97:12	denotes 296:9	133:24 267:14	335:3
110:15	219:6 303:24	depended 120:9	268:1 483:17	determine 218:8
Dawn 3:3 81:2	518:19	120:16	484:5,14	326:7,19 343:7
day 145:23	deeper 123:12	depends 112:20	description 5:13	351:18
169:11 250:20	deeply 123:6	242:23 353:20	6:5 7:5 8:5 9:5	determined 28:8
250:21,24	399:16	495:4	111:20 160:5	345:8
251:1,3,4	defendant 3:20	deponent 11:12	451:8	determining
340:7 342:16	4:6 12:21,24	41:2 520:2	design 170:13	20:16 218:13
352:18 431:11	14:1	deposed 14:22	170:21 196:9	218:16
473:17 520:20	defendant's	41:6	211:10 229:14	detracts 259:13
days 55:21	33:5	deposing 518:16	238:7 241:16	develop 136:1

developed 46:16 79:21 118:14 326:13 385:12 386:3 423:2	321:13 456:3 461:23 479:17 505:23 506:18	Dineo 461:3	disclosures 208:19	79:18 122:23 123:5,10
developing 17:17 65:10 115:14 174:23 326:15 342:4	differences 216:3	direct 228:14 425:14 517:21	discounting 277:2 278:10	DISTRICT 1:1 1:2
development 20:2 21:10 331:8 336:19 338:16 351:5 374:16	different 35:10 41:16 42:13 45:24 46:5 64:4 74:7,8 83:4 94:8,18 94:23 113:5 128:17,18 139:10 149:19 157:15 215:23 219:7,14 227:16 231:9 231:10,11,12 233:13,20,21 233:22 240:5 241:7,12 247:18 248:5,7 248:7 261:22 261:23 266:20 282:2 285:24 289:14,15 298:21 305:14 336:18 366:5 368:5,7,11,13 381:1 399:7 426:5 429:17 430:20 449:20 456:4 471:2 483:18 506:1,3 506:5 511:2	direction 10:5 194:7 226:18 226:23 directionality 370:21,23 372:1,2 directly 81:21 457:6 director 427:3 428:10 disagree 33:10 77:1,3 80:19 81:19 86:3 89:11,16 99:18 138:21 156:7 156:10 169:19 179:12 183:21 207:3 218:3,24 221:5 258:2 261:3 264:17 297:15 306:9 335:6,11 394:13 395:14 401:7,12,17 402:1,6,7 420:22 426:8 426:11 428:5 433:24 434:3 445:12 457:2 464:5 disagreed 86:10 88:13 98:12 306:12 disagreeing 92:3 426:24 428:8 428:13 disagrees 168:14 328:6 disappears 451:24 disclose 207:24 479:8 disclosure 154:23	discovered 306:21 discrepancies 409:2,9 discrepancy 89:8 discrepant 407:11 408:20 410:8 discuss 100:20 170:13,21 172:19,24 173:6 discussed 172:22 discusses 135:23 147:6 discussion 81:13 172:11 293:12 374:6 481:15 508:24 disease 21:11 158:11,13 206:11 210:18 335:1,3 487:14 disingenuous 182:7 dismissal 201:11 dismissed 210:14,19 dismissing 210:23 212:22 dismissive 132:23 disparate 296:17 disparity 364:20 dispute 244:13 disrespected 214:5 disrespectfully 213:23 distinguish	divide 204:19 Docket 9:7 doctor 12:2,8 13:13,19 14:12 15:8 22:1 23:18 26:14 31:9 32:2,12 37:9 39:16,21 40:3,9 41:10 41:23 45:9,11 46:1 52:6,22 59:13 60:12 61:21 63:17 64:11,19 66:11 67:21 69:23 70:9 72:3,4,17 73:12 74:5 75:4,22 76:7 76:22 79:4 80:9,19 82:2 83:15 86:20 88:4 89:14 93:4,20 96:5,9 101:12 102:17 104:10 110:11 110:18 122:15 126:18 129:18 131:12 133:8 133:10 134:7 135:14 136:2 138:16 139:12 141:3,8 144:11 144:19 146:13 147:10,22 150:16 155:17 158:20 159:9 159:22 160:10 161:16 162:7 163:8 165:5,20 166:7,19 167:10,21 168:21 169:23 170:6 171:5
develops 326:9 diabetic 36:11 diagnosed 25:2 25:12,22 391:12 diagnosis 14:14 79:11,13 256:20 353:3 diagram 281:5 281:10,12,22 282:4,8 diaper 29:24 diapered 29:18 30:4 32:14,21 diapering 346:15 399:8 diaphragms 236:20 dichotomous 477:4,5,5 Diego 2:9 differ 491:15 difference 42:15 59:18 79:2 158:16 183:18 185:6 201:20 201:21 202:15 217:14 222:8 222:10,11,15 222:17 230:14 230:20 254:22 261:19 262:17 279:24 280:2 295:23 321:2	differentiate 122:10 differently 158:24 283:24 388:21 492:6 difficulties 78:24 difficulty 185:16 389:21 dilemma 469:12 dilute 291:24 diluted 290:22 291:20			

173:9 179:11	406:18 407:3	110:4,12	dose 389:14,23	118:5
180:2,10 181:9	408:4 409:18	111:14 114:20	391:19 471:5	drawing 216:2
181:12,17	410:5,17	115:2 180:4	dose-response	drill 48:23
182:20 184:9	414:17 415:1,8	186:6 199:23	339:18 340:3	DRINKER 3:7
186:3 189:23	417:12,24	210:8 220:14	345:8 389:19	drive 2:4 3:8 4:3
190:5 191:14	418:7,16,24	224:5 255:14	390:5,7,7	232:19
192:8 197:21	419:2 420:9	271:10 273:23	470:6,14,22	driven 127:15
198:24 199:9	421:23 422:18	292:17 302:9	471:1,6 475:3	128:22
199:10,17	424:18 427:12	302:14 333:21	475:4 476:18	drop 236:6
200:5 201:2	429:10 430:6	344:3 363:14	476:23 477:7,8	495:16 513:4
203:8 206:7	430:21 431:2	377:15 403:21	477:12,14,17	DropBox 106:22
208:6 209:5	431:12 432:17	406:21 407:17	douching 8:14	dropped 311:5
210:7 211:12	434:12 437:18	407:22 424:10	405:8,11,15	495:10
212:11 215:14	439:17 441:18	424:15,18	download	dropping
216:20 218:19	442:22 443:18	425:4 429:2	106:20,21	326:14
220:18 222:20	446:10,13,15	463:11 468:2	107:2,4 503:10	drops 193:24
228:6 229:18	446:22 447:16	471:7,20	downloaded	drug 33:22 34:8
233:4 239:22	453:5 454:4	486:12 488:9	107:1	34:9,11 35:14
244:10,19	455:9 456:22	488:10 490:21	downloading	243:24 453:16
256:1,4,10	457:19 459:19	496:19 497:14	107:7	dry 36:13
257:4 258:20	464:16 465:10	503:1,6,11	Dr 11:13 54:10	DSAR 143:20
269:12 270:5	465:21 467:22	documented	54:20,23 55:3	dubbed 210:10
271:16 272:19	470:4 471:13	432:2	55:6 81:20	due 263:15
274:4 279:11	471:14,24	documents 10:8	110:17 111:11	317:16
280:20 293:3	472:19 474:2	38:10 103:3,9	124:20 125:4	duly 11:20 517:5
294:21 295:22	475:14 476:8	103:13 104:18	135:22 137:20	duplicates 150:3
302:15 303:15	477:16 479:1	105:17 107:11	140:12,15,17	duration 339:19
306:11 308:22	479:24 480:2	110:23 116:20	140:24 142:23	343:4 351:19
316:1 322:2	480:21 485:16	117:2 119:13	143:8,13,14	376:8,13 384:6
327:20 331:6	486:9,16,24	154:6,12,21	146:9 156:17	388:4 389:5
334:3,8 335:20	488:8 489:8,14	155:12	156:17 157:4	472:20 474:4
335:24 336:14	490:9 491:2,11	doing 15:20	168:3 170:7	474:10 475:20
340:16 341:19	494:18 495:19	47:10 66:7	185:16 207:24	476:2
344:1,9 348:18	497:1,19	81:2 92:19	209:16 263:16	dust 71:11 128:9
350:16 353:13	502:15 503:9	138:7 153:24	285:22 294:2	dusted 130:2,16
354:5,12	503:13 507:2	194:2,10 195:9	298:14 340:23	330:12 390:17
356:16 357:13	510:11 513:11	216:9 219:21	369:22 412:8	439:2
358:6,8 363:20	514:8 515:21	226:7 231:9	426:1,12,15,22	dusting 134:3
365:17 367:21	doctors 156:24	300:1 321:21	426:23 428:9	236:20 390:2
371:7 374:8	204:21 219:18	336:9 350:9	461:1,3 478:10	396:13
375:13 376:12	219:23 235:22	429:3 450:8	490:4 493:4	Dusts 5:22
377:3,20 378:4	294:22 372:7	461:8 464:2	495:11	
382:12 387:14	426:4	475:6,9 477:8	draft 6:19	E
393:2,15	document 1:8	483:10 499:19	142:13 143:12	E 5:2,10 6:2 7:2
397:11 401:15	40:12 45:5	502:11 504:22	144:3,17	8:2 9:2 519:1
404:1,11,14	64:13 71:4	504:23 513:7	220:11	e.g 84:3 259:5
405:8,19	102:13 104:21	518:8	drafting 111:21	earlier 80:24,24

88:12 204:2	efficacy 34:15	endured 35:3	336:3 357:17	373:19
266:14 269:10	effort 122:23	engaged 28:12	378:12 410:19	estrogen 205:18
294:23 318:10	efforts 203:5	engagement	413:12 452:7	243:9,12,13
338:21 348:3	453:22	59:10,21	459:24 462:3	et 88:19,19
352:15 362:24	effusion 468:17	engine 120:2	487:1,7,20	255:19 303:4
371:7,17	468:19	Engineering	Epstein 9:6	358:4 416:11
392:15 397:2	effusions 9:11	446:19	426:1,12,15,22	416:23,24
409:14 410:3	466:10 468:1,7	enrolled 383:16	equal 241:23	417:5,14
413:13 414:23	469:11	enrolling 340:13	398:6	453:14,18
425:21 444:10	egregious	entail 43:21	equally 204:1	462:10
444:11 451:16	144:16	112:19	311:18 369:16	ethnic 248:9
515:11	either 127:10	entailed 44:1	equivocally	ethnicities 240:5
early 30:10,18	198:4 278:9	entire 68:15	202:20	evaluating
31:18 32:15	286:10 326:2	214:16	eradicating	491:3
151:5,18	329:13 350:12	entities 3:15	217:11	evaluation 94:3
352:10 487:9	368:22 440:24	entitled 52:7	ergo 300:4	161:21 224:18
earned 114:6	506:2	139:8 155:18	err 506:20	477:6
easier 75:7	electronic 106:4	191:4	errata 518:6,9	evaluations
498:10	electronically	entity 262:21	518:12,15	224:15,16
EASTERN 1:2	105:15 106:15	entry 444:10	520:12	225:12 227:23
EBM 7:19	106:24	environmental	error 355:7,15	event 473:19
302:18	elevated 348:5	61:4 88:8 89:5	errors 203:4	events 432:12,19
echo 260:9	349:3,9,19,23	EOC 347:15	407:24	ever/never
Ed 185:9,11	353:17	487:11	especially	415:9,12 416:6
200:24 329:10	Ellen 156:18	epidemiologic	226:13	416:10 417:10
489:20	292:4	56:22 115:17	ESQ 2:3,8,13,13	everybody
editorialize	ELLIS 4:2	137:7 149:7	3:3,8,12,17 4:3	177:23
280:21	Elmo 73:7	164:16 288:8	essence 59:19	everyday 389:16
Eds 185:12	181:18 281:9	359:22 392:15	established	389:17
educational	463:9 464:8	485:10	87:20 139:21	evidence 19:13
23:5	embedded 123:7	epidemiological	335:1 365:22	49:10 63:12
effect 15:10	399:16	57:10 165:6	379:6	128:4 158:12
182:24 183:14	employed 160:2	262:4 273:16	estimate 193:22	175:19 176:3
185:21 205:1,5	161:5 173:1	288:20 359:17	196:16,17,21	182:8 217:22
205:17 217:6	469:16	360:2 492:13	197:2,2,13,17	255:11 280:12
290:7,14 314:4	employee 301:2	492:16	197:18 203:24	281:6,11,14
314:9 318:16	endeavor	epidemiologic...	226:22 264:14	282:14,24
318:22,24	103:11 496:14	358:22	347:14,24	283:12 302:24
324:3 330:20	503:14	epidemiology	349:10,16,18	305:6,6 315:3
339:17 367:6	endeavored	7:14 154:3	349:19,23	336:22 394:21
420:19 421:3	115:9	164:23 286:22	371:4 474:17	395:21 398:10
436:9 452:13	ended 78:22	287:2,4,7	estimated 336:4	412:8 422:8,12
509:3 510:9	Endnote 229:18	392:9	estimates	422:16 428:20
effects 22:3	endometrioid	epithelial 7:6,22	187:20 354:2	429:4 430:8
201:11 204:24	409:5	8:9 9:15 21:17	estimating	432:6,6 436:20
210:14 212:23	endometriosis	249:18 276:15	337:1	437:6 448:7,12
450:22 454:12	487:13	280:16 311:23	estimation	449:2,15

450:21 451:3	498:8	503:2,6	119:18 120:12	185:20 216:9
451:18 453:24	examples	exhibits 54:7,11	121:3,7 123:15	252:22 253:12
458:20 479:21	205:16 267:14	54:15,20 55:5	123:21 124:1,5	257:15 258:7
481:12 482:5	314:20,21	55:12 119:18	124:18 125:2	263:11,13
484:13 505:20	455:3 457:22	142:24 143:9	126:19 127:4	272:9,21 273:9
508:3,10 509:3	457:24 458:1	143:14 146:9	127:18 134:8	297:23 460:9
510:23 511:7	exception 192:9	147:3,10,14,15	135:21 139:15	460:11 461:20
511:23 512:12	Excerpt 5:14,16	147:19	139:20 140:15	462:22 511:21
Evidence- 7:19	5:19	exist 41:17	140:17 146:17	explained 78:6
evidence-based	excesses 93:12	130:4,19	147:1 148:2	98:12 314:2
281:15 283:10	excuse 96:14	492:14	150:22 155:14	356:23 440:1
302:17,22	190:5 327:6	existing 43:13	157:1,7 162:17	explaining
303:5,17,19	463:6,7,15	exists 425:13	180:3 184:23	199:2 267:16
305:2	Excused 516:6	491:13 492:12	186:4,11	314:24 353:10
exacerbated	exhaustive	expand 77:16	187:17 208:1	460:21
335:2	492:1	expect 185:22	208:13,16	explains 196:7
exact 88:22	exhibit 39:19	225:21,24	242:20 243:5	explanation
91:17 266:12	40:7,13,21	226:8 227:15	271:8 273:4	167:4 254:21
285:20 481:15	45:6,10,11,19	259:21 260:14	274:4 276:19	263:19 331:2
484:7	55:10 64:12,14	339:15 410:13	281:2 292:5	399:4,6 480:11
exactly 50:16	71:5,9 72:20	expelling 422:8	303:7 308:23	explanations
51:22 86:9	102:12,14,18	experience	309:4 315:6	252:24 400:12
117:11 129:23	110:5,8 114:21	78:20 178:13	352:2 353:8	explicitly 90:6
141:22 168:16	115:1 121:8	341:12,15	355:5 356:17	exposed 17:22
218:14 244:9	146:12,20	experiment	375:5 405:23	254:17 341:7
255:4 280:3	150:21 180:5,9	280:1,7,9,13	407:4 411:16	342:18 346:14
349:15 356:4	186:5,7 199:24	433:22	502:16,22	368:20 384:7
395:4 406:16	200:4 220:12	experimental	515:3,8,13	exposure 7:6
440:2 460:10	220:15 224:4,6	145:6	expertise 302:24	20:1 21:9
475:17	255:15,19	experiments	504:8	26:15,20 27:7
EXAMINATI...	258:22 269:20	22:2	experts 127:19	27:19 28:7
11:23	271:11 273:24	expert 6:10	129:20 130:15	60:14 61:13,17
examine 411:5	292:18,22	12:20 37:10	132:10 140:5	61:22 62:15,22
examined 11:21	302:10,13	38:15 39:11	149:5 156:11	63:4,13,18
80:6 93:15	333:22 334:1	49:13,21 50:11	156:12 157:4,6	65:1,5 67:7,23
437:15	344:4,8 363:15	50:19 51:5,6	157:9 158:23	68:1,18 70:2
example 19:13	363:18 377:12	51:16 52:24	198:19 210:22	70:11,18 71:1
36:10 132:4	377:16,22	53:19 54:5	214:21 215:2	72:13 74:16
135:22 157:23	403:20,22	57:13 58:13,22	292:3,14	80:5 82:19
205:12,13	406:22 407:2	59:5 86:20	experts' 50:7,9	83:16,19,21,22
207:16 226:7	407:18,22	87:3 104:11	52:1 53:12	84:4,8,12
248:10,16	424:11,15	105:6,18	58:13 172:14	87:19,23 88:9
264:20 281:24	428:16 468:3	107:12 108:10	173:3	95:14 149:9
290:4,18,21	468:10 471:8	110:14,20	expires 520:21	220:24 224:20
291:18 381:11	471:12 486:13	111:6,16,21	explain 137:15	237:23 252:2
395:18 409:4	488:9,11	112:2 115:1	137:24 161:12	252:10 256:19
425:20 494:14	496:20,24	118:3,5 119:3	167:1 168:15	259:5 280:5

310:1,21	F	123:22,23	502:14,17,23	field 215:2
311:12,24	F 3:18	137:9 150:16	503:7,14,15,22	fifth 1:14 11:9
323:13 326:8	facilitate 173:12	150:19 157:7,8	503:24 504:13	305:8
326:17 330:10	fact 41:13 69:20	167:20 189:5	505:3	figure 101:6
331:23 332:7	78:13 160:16	202:10 209:10	FDA's 495:20	262:19 281:1
335:18 336:18	161:2 179:1	262:18 263:9	496:2 497:2	282:19 283:3
337:15 338:15	204:10 206:14	264:5 269:1	498:24	336:11 361:15
339:10 342:13	232:1 236:7	295:14 312:14	FDA.gov/cos...	362:4 400:17
344:12,16	254:11 272:16	409:13 466:6	497:3	415:16,18
353:2 354:1	281:13 287:16	475:18	fearing 513:6	418:3 475:8
366:20 367:9	288:13 317:14	fairly 311:18	February 49:14	file 103:23 104:1
376:2 384:6	324:19 360:1	fall 36:20,24	104:12 108:5	104:10,22
390:23,24	361:12 369:16	284:16	115:3 124:6,19	106:18 107:6
391:4,23 394:4	380:5,11	fallopian 422:4	125:3 147:2	files 103:16
394:4 397:4,5	381:15,23	422:21 423:15	151:5	final 118:12
404:4,6,15,16	395:2,2 396:22	438:17 443:20	federal 504:7,20	144:15
415:8,11	403:2 414:7	452:8	feel 92:21 214:4	finally 144:5
417:11 420:10	432:18 435:14	falls 340:2	246:2 297:7,16	215:15 216:24
420:17 432:10	442:13 444:8	391:15	392:11 492:6	217:9
444:12,14	448:1 449:11	false 178:7,15	511:16	find 36:13 68:16
470:20 513:7	459:15 461:12	204:7 210:9	feeling 45:4	91:16 93:18,23
exposures 61:4	480:10 511:19	falsifying	168:17 310:3	94:12,14 128:4
61:19 86:5	factor 17:10,14	179:18	509:13 511:9	128:12 129:17
98:15 272:17	18:19,20 23:23	familial 456:6	fellows 23:7	130:8 131:13
316:13 337:21	24:9 243:11	familiar 204:22	fellowship	134:5 141:1
expound 222:2	405:11,15	267:11 287:13	284:11	150:9 160:8
expressed 318:9	487:20 507:12	familiarity	felt 164:9 190:1	165:7 179:21
461:13,14	factories 63:9	262:12	190:13 290:13	185:15 195:22
expression	factors 8:9 23:4	family 341:13	489:22 513:8	196:6 205:4,6
459:24 460:19	23:10,20 24:7	487:11	female 25:3	222:7 238:13
461:18 462:3	24:23 25:14,24	far 53:10 95:21	173:11 365:24	265:23 274:15
extend 80:4 86:6	26:9 158:24	214:18 238:8	366:2 422:24	280:15 282:7
extending	243:5 246:5	346:2 444:24	427:6 445:15	282:15,19
100:11	251:23 271:20	504:11	Ferante 88:18	283:1,3,9,16
extensive 91:2,9	271:23 296:10	fashion 35:7	fiber 42:13	286:3 288:4
extracted 417:3	296:14 487:7	faster 120:22	397:7,13 398:1	292:12 309:11
extrapolate	factory 69:10	430:5	fibers 41:16	311:19 312:21
337:3	332:18 369:15	fax 1:20	42:21 65:9	314:20,21
extrapolated	facts 107:19	FDA 9:6,19,22	74:7 75:16,18	315:3,5,7
353:5	fail 518:18	424:16 426:8	76:3 85:1,7,17	317:15 320:23
extrapolating	failed 93:18	426:14 428:5	85:20,22	321:9 337:14
336:10	failure 217:15	496:2,14 497:8	Fibres 5:22	342:3,5 367:20
extrapolation	fair 16:7,8,19	497:20 498:21	71:11	391:11 392:2
331:20,20	21:15 38:19	498:22 499:3	fibrous 109:1	446:1 453:24
extrapolations	41:14,20,22	499:14,18	170:9 478:17	463:10 480:14
333:11	42:20 113:21	500:8 501:4,11	482:12,16,23	506:7
eye 36:7 270:13		501:16 502:12	483:13,24	finding 61:1

77:17 93:14	127:8 164:7	361:16 364:15	104:24 106:9	245:23 246:8
101:5 131:8	182:19 199:16	368:15 373:2	108:13 109:8	246:23 248:4
165:1 187:7	213:11 214:20	373:22 382:9	109:16 112:16	249:8,23
196:4 256:21	224:22 237:1	506:10	113:23 116:22	250:12 251:15
263:13 280:15	260:2 264:15	following	117:8,24	252:13 253:3
290:14 357:15	266:8 275:16	115:20 334:4,7	118:19 119:6	253:22 254:10
370:13 371:1	287:8 295:2	339:3	121:10 122:7	257:13,22
371:10 372:18	319:12 320:3	follows 11:21	122:17 124:12	260:1 262:9
391:23 395:7	321:21 323:1	Food 427:3	127:21 130:21	265:6 267:9
396:6 434:13	325:11 326:19	428:11	131:24 136:14	268:14 273:1
434:17 497:20	327:23 328:17	footnote 334:4	137:3 139:24	277:19 278:17
findings 61:5,8	365:20 377:5	488:4	142:4,17 143:4	279:3 282:12
67:4 80:3 86:7	407:14 425:4	force 15:9	146:7 147:6,12	283:14 286:17
89:2,12,17	430:17 443:18	forced 284:8,9	150:18 152:8	288:1,10,24
91:17 92:17	461:19 469:6	foregoing	153:9 155:3	289:22 291:5
178:23 179:13	476:9 479:7	517:18 520:6	156:4,15	295:16,18
179:21 205:14	FISH 3:3	foreign 240:14	157:18 159:2	296:3,21 299:1
241:24 256:16	five 61:16 62:8	240:17 423:3	159:17 160:21	300:19 302:2
259:12 272:10	87:21 89:3	forgot 31:9	161:8 162:1,20	303:13 304:15
275:22 276:7	217:3 376:10	308:18	163:1 165:12	305:17,23
280:3 303:24	471:19	form 16:24	166:3,10	307:8 308:13
307:24 358:10	flashes 37:4,7	17:13 18:2,12	170:17 171:13	312:3,16
358:17,18,24	flaws 293:15	19:2,20 20:20	172:2,8,18	315:16 316:7
359:19 373:20	313:1 319:21	24:2 25:16	173:5,15 174:5	316:23 317:19
379:16 395:6	flipping 310:8	26:3,23 27:14	175:22 176:5	318:6 319:9
419:14 433:21	Florham 3:9	28:4 29:3,21	176:10 177:5	327:13 330:8
435:2 436:19	fluid 151:19	30:20 32:18	177:19 179:6	331:12 333:2
fine 66:7 73:4	468:19	33:8,14 34:18	185:3 188:5	335:8 338:7,14
126:2 401:19	FLW 1:6	35:1,7,16 36:2	192:4,18	340:21 341:9
finish 52:18	focusing 68:12	38:23 39:6	193:13 195:6	342:11 343:9
92:12 133:16	folks 498:11	42:4 43:23	196:19 197:5	343:13 344:20
133:18 138:24	follow 313:22	44:20 45:21	198:14 202:8	345:12 346:6
163:10,21	338:1,10 339:6	46:3 47:3 48:7	203:14 204:13	346:17 349:6
166:13 233:2	380:13 458:1	49:18 50:15	207:2,13 211:4	349:21 355:11
237:16 306:16	495:17	51:3,20 53:5	211:6,16 213:4	355:13 356:21
310:17 327:23	follow-up 20:16	55:23 56:12	213:6 215:4,10	358:12 359:2
328:16 332:8	325:13 350:1,3	57:20 58:9	216:7 218:5	359:11 360:17
332:11 447:1	350:15 351:2	60:6,17 62:1	219:11 221:7	362:11 364:6
462:19 463:16	352:14 353:2	62:18 63:1,22	221:22 223:5	364:13 365:9
finished 79:7	355:18,20,23	65:17 66:5	225:4 230:11	366:7 369:8
133:11 485:22	356:2 361:18	70:5,13 77:5	231:5 232:16	370:19 372:21
516:1	363:22 368:16	84:14 89:22	234:17 235:8	375:21 379:21
first 11:20 12:23	379:6,14	90:23 92:1	235:14 236:23	381:8 382:24
21:9 33:17	404:22	95:5,20 96:13	238:1,21	385:7,20 386:7
37:22 43:3	followed 293:23	98:8 99:21	241:14 242:3	387:6,16 388:7
87:14 103:1	311:4 339:8	101:21 102:8	242:14 244:2	388:15 391:8
121:23 122:2	340:5 356:6	103:20 104:14	244:15 245:9	393:8 394:9,15

395:16 397:16	49:11	270:15 343:4	50:23 51:8	156:6,19
398:4,24	formulating	344:17 345:9	52:5,14,17,21	158:18 159:8
399:20 400:4	52:9 107:21	376:18 404:6	53:17 54:1,12	159:17,18
401:10 402:3	155:13	404:20 474:4	55:1 56:1,13	161:1,15 162:2
402:11 406:2	forth 108:5	475:20 476:3	57:24 58:4,15	162:21 163:7
408:18 410:22	350:3 401:6	frequently	60:8,19 62:13	163:15,17
412:14,22	406:11	343:1	62:20 63:15	165:4,13 166:6
413:22 414:20	forward 54:16	fresh 28:24	64:10,16 65:19	166:17 167:15
417:17 419:9	471:20	Frey 242:8	66:3,8,10	168:20 169:2
419:22 423:18	found 47:7	front 40:20 41:1	67:18,20 68:6	169:17 170:1,5
427:20 431:9	75:17 76:3	45:12 211:18	70:6,7 71:7,18	170:19 171:14
432:22 433:7	80:1 85:18	271:15	72:2 73:3,5,16	172:3,12,23
434:2,20 435:7	94:21 95:15	frozen 450:11	73:21 74:4	173:8,17 174:8
436:17 438:3	177:24 217:4	frustrates 209:6	76:16,21 79:3	176:1,6,15
439:10,12	228:18 237:12	full 39:24 71:14	80:8,14,18	177:8 178:12
440:12 441:12	276:4 280:11	71:20 74:2	82:1 84:15	179:10 180:7
442:1,11 447:5	280:11,18	87:14 91:22	90:17 91:20	183:9,10 186:2
448:4 451:6	282:5 307:24	127:8 138:17	92:4 93:1	186:9 188:6
452:22 454:22	310:23 321:1	148:11 155:11	95:17,23 96:15	190:11,22
459:11 460:4	323:5,16,18	164:20 203:16	99:17 101:11	191:13 192:7
462:6 464:21	373:17 376:22	232:23 443:18	101:24 102:9	192:19 194:11
468:9 469:3	378:10 390:20	443:19	102:16 103:4,7	195:12 196:24
470:16 475:24	391:4 409:4,6	further 45:3	103:22 104:16	197:9 198:23
477:21 480:6	409:7 436:12	76:14 110:23	105:3 106:11	200:2 202:9,24
481:3 482:19	443:4 453:21	203:20 383:12	107:17 108:15	203:18 204:14
484:20 485:5	454:16 477:12	420:17 442:20	109:11,19	206:4,6 207:5
487:23 489:10	482:12 505:11	449:10 463:19	110:7 112:17	207:14 208:3,5
491:6,18 493:1	foundation	504:14 515:20	114:1,23	208:23 209:13
494:12 496:8	155:19		116:24 117:14	209:20 210:6
496:17 497:24	four 13:20	G	118:4,24 119:8	211:11,23
499:9 500:3,14	112:23 161:2	game 390:4	121:12,18	213:10,17,20
500:22 501:9	161:10 273:5	Garber 2:3 5:5	122:13 123:3	214:3,6,13
504:17 505:7	273:12 305:8	12:1 17:2,18	124:16 125:1	215:5,13
506:22 507:24	356:17 357:8	18:8,17 19:15	125:23 126:4,8	216:13 218:17
508:17 509:24	369:18 376:10	20:5,23 24:12	126:17 129:7	219:15 220:17
510:19 512:4	405:22 406:11	25:17,19 26:12	131:11,21	221:8 222:19
512:23 513:13	489:5	26:24 27:5,23	133:7,14	223:7,21,24
514:11,17	fragrances	28:15 29:7	136:19 138:15	224:8 225:5
520:10	109:14	30:1,21 31:4,8	139:2,9,11	230:24 231:8
formal 26:5	frame 264:11,13	32:10,23 33:11	140:3 141:20	233:3 234:20
format 285:1	264:24 336:6	33:20 34:19	142:6,19	235:10,18
formed 24:11	fraught 285:7	35:8,19 36:18	143:10 144:8	237:18 238:17
44:14 47:19,24	289:18	39:2,15 40:1,2	144:10 146:10	239:3,13,21
345:23	free 108:18,24	40:5,11,15	147:8,21	240:24 241:2
forming 108:2	256:20	42:19 44:5	148:13,16	241:17 242:5
117:16,20	French 487:3	45:8 46:21	150:20 152:11	242:16 244:5
formulated	frequency 29:23	47:4 49:9 50:5	153:14 155:5	244:18 245:13

246:1,11 247:5	377:8,13,18,24	483:4 484:23	83:19,21,23	365:7 366:21
248:22 249:12	378:3 380:20	485:15,19	84:5,13 85:6	368:6 372:11
250:3,13 252:6	382:2 383:3	486:8,15 488:3	110:15 158:7	372:18 373:17
252:18 253:6	385:14,22	488:13 489:13	177:24 178:21	378:24 379:10
254:1,23	386:11 387:7	491:9 492:8	270:24 271:5	379:17 380:5
255:17,22	388:1,11 389:1	494:5,17	314:16 320:6	380:10,14
256:3 257:16	393:1,11	496:11,22	330:1 356:23	382:21 383:5,8
258:1 261:2	394:12 395:10	499:2,11 500:7	406:5	403:12 411:18
263:23 266:5	396:9 397:20	500:18 501:1	generally 32:11	411:23 412:11
268:8,16	398:14 399:1	501:23 503:4	37:24 137:16	413:11,19
271:13 273:3	399:24 400:23	504:24 505:8	141:2 177:3,15	415:9
274:2 276:3,6	401:14 402:4	507:1 508:8	241:12 245:7	getting 59:12
278:6,23 279:7	402:14 403:24	509:17 510:1	246:24 247:1	75:2 77:7
282:22 283:15	406:6,24	511:24 512:7	313:14 320:4	226:24 254:13
286:19 288:5	407:20 408:3	513:9 514:7,14	genital 9:13	255:7 318:19
288:11 289:9	408:19 411:1	514:21 515:17	173:11 280:16	389:18,24
290:1 291:8	412:17 413:2	515:24	311:24 357:17	390:1,3 391:14
292:20 295:21	413:23 414:21	gas 63:7 69:8	374:16 419:5	Ghio 9:12
296:5,22 298:2	415:2 417:20	78:1 332:17	423:1 427:6	465:22 468:23
299:3 300:22	417:23 418:21	369:14	437:20,24	girls 88:7
302:7,12	418:23 419:10	gate 48:2	438:15 445:15	give 78:18 88:17
303:14 304:17	420:3 421:13	Gates 8:11 48:3	448:9 476:15	99:5 121:24
305:18 306:2	421:22 424:4	149:12 207:16	genitals 28:24	128:15 132:11
306:18 308:6	424:13 427:24	311:4 324:13	29:10 30:10,17	141:15 194:12
312:6 313:13	430:23 431:1	324:15,17	31:17 32:5	195:19 205:15
315:17 316:10	431:10 432:24	339:7 356:1,2	33:6 131:18	212:1 228:10
317:2,21 319:2	433:9 434:11	357:14 358:4,8	134:21 135:16	228:11,13,17
321:15 327:19	434:24 435:22	359:18 360:14	135:17 174:3	232:23 266:12
328:8 331:5	437:17 438:12	360:19 361:21	239:8 384:22	348:8 395:17
332:9 333:5,24	439:16 440:15	362:8,17,21	404:7,16	409:16 417:13
335:10 340:15	441:17 442:4	363:1,13,19,20	439:23 441:22	417:13 421:10
341:1,5,17	442:21 446:7,9	364:3,11,22	479:6 482:17	421:11 425:1
342:12 343:10	447:15 449:17	365:6 366:17	484:2 501:6	425:11,12
343:15,24	452:5 453:4	367:13 368:14	507:22 512:20	430:2 438:20
344:6,22	454:3 455:8	370:5 372:12	genuine 210:14	472:13 473:5
345:13 346:9	456:18,21	372:18 373:9	212:22	485:13 494:16
346:20 348:17	457:3,8 459:2	373:15 379:10	Gertig 8:8 48:3	494:18,21
349:17,24	459:12 460:6	379:16 380:10	135:8 149:13	508:5 512:17
350:23 354:11	462:9 463:4	381:24 382:4	248:16 310:22	513:24 515:18
356:13,15	464:15,23	382:12 411:18	344:2 347:2	given 15:15
357:1,6 358:15	466:24 468:5	411:23 412:10	356:18 357:10	50:11 53:18
359:3,14 362:2	468:15 469:5	413:10,20	358:1,10,19	73:1 138:4
362:18 363:17	470:1,3 471:10	414:3 415:11	359:19 360:3	181:13 182:3
364:7,19 365:3	472:14,18	416:9	360:10 361:20	182:24 183:13
365:10 366:11	473:7,20 474:1	general 6:11	361:23 362:20	241:21 262:2
369:24 371:6	476:7 477:24	21:5 23:5 26:1	363:23 364:4	285:16 286:2
373:24 376:1	480:20 481:7	26:8 38:1	364:12,16,22	288:13 297:8

325:11,12,17	417:24 431:24	220:8,10	239:23 264:20	101:19 102:2,4
326:23,24	432:5 440:22	226:18 228:8	267:12 285:11	211:9 226:10
337:8 341:3	441:3 445:3	228:10,11,13	350:12 386:4	238:3 248:9,10
389:6 481:19	453:5 455:12	232:19 243:2	391:21 416:3	272:6 311:3
517:6 520:8	457:11 459:7	255:18 260:21	Google 120:4,18	312:10 315:10
gives 331:1	473:7 476:8	265:18,20,22	120:20	320:7,8 321:12
386:4 504:19	484:16,21,24	265:24 270:17	Gotshal 1:14	321:19 346:13
giving 24:5 26:8	485:23 489:16	271:4 274:3	3:12	346:14 356:6
178:7,22	503:14 508:19	285:10,11	government	373:2 385:18
179:16 337:19	509:5 510:12	292:21 316:17	145:2	397:13 398:2
372:23 463:19	511:5	319:13 320:15	grade 449:13	398:22 491:14
494:23	goes 65:7 86:2	320:16,20	451:13 461:12	492:11,21
glad 441:2 447:8	88:3 97:22	321:17,22	gradient 477:19	groups 92:16
447:16	183:24 201:8	324:21 327:17	graduate 284:10	201:20 322:9
glean 122:14	214:19 263:8	328:16,23	grant 145:13	grown 250:19
gleaned 122:19	287:10 323:10	330:4 337:24	granuloma	guess 16:3 28:10
gloves 400:8	338:19 378:15	338:1,4 342:1	449:2	38:5 39:8
go 15:1 31:9	382:10 398:20	344:1 360:8	granulomas	59:18 86:11
50:20 53:14	400:16 434:8	362:3 363:6,7	448:17 450:6	115:19 130:23
54:1,14 65:4	444:16 458:24	372:23 392:23	granulomatous	131:2 149:4
66:11,13 67:3	going 15:17 16:6	397:10 403:15	449:3,16	250:16 280:2
67:14,24 68:12	21:12 30:22	407:1,21	451:20	418:2 426:24
68:14 72:5	39:18,19 40:6	409:16 410:12	gravel 87:6,9	427:7 475:16
88:18,20 94:2	43:15 45:9	417:21 424:14	Gray 1:15	493:23 502:2
94:6 98:3	59:13 61:7	428:14 435:21	517:12	guidelines 305:6
99:12 100:14	64:6,11 65:20	451:3 453:7,10	great 170:3	guilty 120:20
112:20 129:16	66:24 67:11	456:24 458:4,6	214:2,8 228:16	guinea 130:10
130:7 133:9	71:8,22 72:11	471:11 472:2,5	230:19	guys 126:1
136:16 146:11	75:8 76:4,5	474:14 475:1	greater 194:15	255:24 377:14
161:12 165:8	77:9,21 79:4	480:9 481:9,13	195:16 198:7	GYN 179:23
167:7,8 169:6	99:12 100:13	484:3 485:10	241:23 339:9	242:10 455:20
169:20 182:19	100:23 101:1	485:13 486:9	368:1 370:6	456:10,14
189:14 194:21	114:24 125:13	488:8 493:12	371:9,19	gynecologic
202:11 203:19	125:20 126:11	493:16 494:1,7	376:11 472:21	12:10,14 39:10
206:13 208:4	136:1,3 137:10	494:15 498:20	greatest 293:22	126:20 136:21
209:8 218:1	139:4 144:5	498:23 501:19	Green 232:1	176:16,18,22
237:8 258:20	148:14 159:12	509:12 511:13	233:12 490:14	178:4,14 179:2
269:16,19	164:17 168:7	511:20 512:1	490:22 491:1	180:11 181:4
272:14 275:15	169:22 170:1,2	Golkow 1:20	Greenland	249:14 487:12
285:15 297:22	176:11 180:1,8	11:5	199:18 201:6	507:6
319:3 324:15	185:11,12	Gonzalez 8:16	207:24 209:16	Gynecology
324:22 327:16	189:11,12	48:4 207:9	287:9	488:16 490:1
335:24 361:6	190:7 193:19	403:17	group 30:23	490:11
366:13 367:20	195:1 200:3	good 12:2,3	87:15,17 93:8	
373:9 384:1,14	202:3 205:5,6	15:20 24:15	96:6,11,17,24	H
390:10 397:6	205:7 206:3	125:21 158:12	97:5 98:7 99:1	H 5:10 6:2 7:2
403:4,7 416:17	209:24 216:10	239:10,11,22	99:19 101:16	8:2 9:2

H2O 196:5	182:4	heed 500:1,10	398:1 449:13	487:11
habitual 250:7,8	head 196:1	500:24 509:18	451:13 461:12	Holcomb 1:13
251:1,20 257:1	270:24 441:16	512:1,21	higher 17:16,19	5:4,15,17,20
257:9 258:4	heading 83:20	held 1:14 11:9	152:1 260:13	6:10 11:13,19
263:7 267:22	215:16 217:1	282:1 284:7	272:18 397:8	12:7 54:10,23
338:22	304:4 351:21	318:23	444:14 445:20	110:14,17
hair 469:23	430:14 503:20	Heller 48:4	470:21	168:3 285:22
half 111:12	health 142:13	132:5 134:19	highest 248:14	412:8 517:8
217:4 224:1	143:11,20,23	397:2 398:18	455:24	520:16
232:7 313:8,9	144:4,12,20	432:3 448:11	highlighted	Holcomb's
halfway 74:20	145:23 171:10	Heller's 436:19	293:5	81:20
256:7 271:19	171:20 220:3,5	437:2	highly 200:16,23	Holcomb-1 5:14
275:17	220:10 222:21	help 85:9 101:6	217:17 318:23	40:14
hallmark	256:18 258:21	217:12 250:18	445:5 495:11	Holcomb-10
158:11	261:4 311:8	284:23 365:14	Hill 160:5	6:17 200:1
halt 217:12	324:24 325:9	463:11	161:14 164:5	Holcomb-11
hand 97:10	329:5 331:7	helped 45:3	233:19 246:5	6:19 220:16
handed 53:9	338:18 344:10	79:18	247:11 420:13	Holcomb-12
72:20	363:22 365:21	helpful 52:16	427:15 428:21	6:21 224:7
hands 499:20	365:23 376:22	290:19,23	429:5,12,15	Holcomb-13 7:6
Hang 462:21	378:9 380:21	291:20	430:9,16	255:16
happen 100:8	381:4,20	helps 181:24	431:15 436:6	Holcomb-14 7:9
129:4 132:14	402:15,18	Henry 4:10 11:4	477:18	271:12
267:1 422:12	403:7 413:24	herpes 120:14	Hill's 115:20	Holcomb-15
422:16 424:1	414:2 419:3,17	hesitating 498:6	hired 38:17 42:1	7:12 274:1
happened	420:4,6 427:13	heterogeneity	42:22 43:9	Holcomb-16
337:10 356:5	428:14,19	236:13,18,22	44:7 515:6	7:16 292:19
461:3 464:12	430:7 431:16	236:24 237:8	Hiroshima	Holcomb-17
491:20	436:6 439:20	237:11,20,22	326:14 332:20	7:18 302:11
happening	446:11 477:16	238:5,6,9,11	336:7	Holcomb-18
66:21	494:10	238:14 285:4	histologic 8:10	7:21 333:23
happens 262:13	hear 267:17	319:14 320:19	94:2 259:10,13	Holcomb-19 8:6
427:10 438:8	heard 197:19	320:24 321:5,9	259:16,22	344:5
happily 284:9	201:18 359:4,7	322:13 323:2,5	260:12 450:16	Holcomb-2 5:16
happy 68:14	hearing 6:11	323:11,16,18	histologically	45:7
346:23 434:14	63:17 110:15	323:22 361:3	310:24	Holcomb-20 8:9
434:22 440:22	hearings 37:19	hierarchies	histology 249:19	363:16
441:8	heart 389:19	300:17	historical	Holcomb-21
harbored 44:8,8	400:17	hierarchy 282:1	478:11	8:12 377:17
hard 105:16,22	HEASLIP 3:12	293:19,21	historically	Holcomb-22
106:1 214:8	heavy 28:6	294:4,9,15,16	248:13	8:14 403:23
282:18 283:3	61:16 86:5	294:18 298:17	history 26:5,6	Holcomb-23
285:8 493:3,23	87:22 95:13	301:24 302:6	26:13,16,22	8:17 406:23
hardcopy	98:14 109:5	303:7 304:4,19	27:1,6,17	Holcomb-24
105:19	170:9 326:16	305:2,14	28:11 132:18	8:20 407:19
harm 217:20	331:22 332:7	high 248:24	342:2,6 391:23	Holcomb-25 9:6
hazard 181:13	335:17	260:18 397:13	397:3,4,9	424:12

Holcomb-26 9:8 468:4	301:7,15,16,17 hot 37:4,6	508:6 510:10 512:18 513:16	identical 204:3 identification 40:13 45:6 64:14 71:5 72:14 74:17 102:14 110:5 114:21 180:5 186:7 199:24 220:15 224:6 255:15 271:11 273:24 292:18 302:10 333:22 344:4 363:15 377:16 403:22 406:22 407:18 424:11 468:3 471:8 486:13 488:11 496:20 503:2	important 15:4 49:1 68:11 135:24 137:23 161:17 259:7 260:4 323:11 331:9 343:6 351:14,21 361:8,10 372:9
Holcomb-27 9:13 471:9	Houghton 8:13 48:3 374:9	hysterectomy 442:9 444:13 444:20		impossible 19:7
Holcomb-28 9:15 486:14	375:6,19 376:3 376:21 377:8		I	impressed 495:13
Holcomb-29 9:17 488:12	377:20 379:9 383:13	i.e 84:6 183:2,4 183:15,17		impression 355:21
Holcomb-3 5:19 64:15	hour 60:10 125:20	IARC 5:21 48:4 48:5 61:17 63:5 68:21 69:16,24 70:4 70:10 71:9 77:19 78:4,7,9 79:23 80:11 81:19 88:15 89:1,11,16 91:1,7 92:9,15 94:15,21 95:2 95:19 96:7,20 97:11 98:19 99:2,19 100:10 101:15,18 224:15 225:7,9 225:11,17,17 227:2 228:3,20 229:1,4,10,12 229:16,19,21 247:19 272:5 419:12 420:1 420:22,24 491:3,12 492:10,19 493:5 494:1,9 494:13 495:6,8 495:14,16 510:22 511:3		impressive 460:21
Holcomb-30 9:19 496:21	hours 59:7,23 60:4 112:1,12 112:18,21,22 114:11 214:20 354:23			inability 390:13
Holcomb-31 9:22 503:3	HPV 120:14			inaccuracies 282:4
Holcomb-4 5:21 71:6	HRT 242:22 243:6,11,16,18			inadequate 351:3 369:3
Holcomb-5 6:6 102:15	Hulfish 3:13		identified 208:15 432:13	inappropriate 208:8 379:13 464:2,4
Holcomb-6 6:7 110:6	human 71:11 82:19 83:16 128:9 130:2,16 132:13 134:16 135:15 136:7 215:17 220:20 325:19		identify 107:19 376:8	incident 327:2
Holcomb-7 6:10 114:22			identifying 48:24	include 117:3 149:12 203:1 413:19 414:6 414:10,12 416:23 418:15 483:21 487:8
Holcomb-8 6:13 180:6	humans 224:21		ignoring 319:4	included 21:16 48:2 54:11 55:19 61:2 165:23 203:24 228:21 229:4 362:15,16,20 362:22 365:5 371:18 379:7 411:17,23 414:2,12 416:12 418:5
Holcomb-9 6:15 186:8	HURST 2:7		II 63:9 69:8,9,9 365:23	
hold 89:14 91:18 141:12 151:13 178:1 190:23 192:23 247:8 247:17 275:7 334:9 367:19 448:6 474:15	hyped 201:10		Illinois 4:4	
holding 296:16	hypothesis 259:14 280:8,9 398:13 433:22 434:4,9		illuminated 293:5	
honest 47:6 90:24 341:10 475:7 493:3 513:4	hypothesize 398:7 424:8		imagine 49:2 106:19 107:1 205:10 493:4	
honestly 177:23 251:16 341:11	hypothesized 430:19 431:18		immunohistoc... 79:17	
hope 407:24	hypothesizing 424:2	IARC's 60:23 61:8 97:2 98:13 228:1 495:9	impact 238:16 324:3 442:19 446:5	
hopefully 169:4 388:22	hypothetical 96:22 330:14 337:20 482:9 482:21 483:9 483:20,22 492:10 493:7 494:16,19,24 495:3 502:6	ICD-9 79:14 idea 21:8 65:12 67:2 389:13,23 392:3 430:3 461:15	impacted 251:21	
hoping 91:1 159:4			imperative 518:14	includes 16:14 75:17 85:19 154:19 202:21 232:3,4
hormone 242:21			implicated 256:14	including 16:20 25:3 222:7
hospital 125:18			implies 303:22 303:23 395:8	

252:1 324:13 360:11,19 362:14 455:3 487:12 492:15 inconsistencies 164:11 392:17 455:2 inconsistency 42:18 184:1 185:21 188:23 307:21 442:18 449:7 inconsistent 150:14 185:23 188:2,13 189:1 190:2 191:10 192:1,6 219:7 223:10 339:20 339:21 392:18 460:12 484:10 incorporated 118:11 incorrect 169:18 increase 67:8 90:4,7,14 174:22 183:3 183:18 187:7 245:19 252:22 254:16 259:22 262:12 269:11 269:17 349:13 376:23 392:10 405:9 465:1 increased 63:13 70:19 78:15 88:24 89:3 94:12,14 95:15 98:17 124:10 149:8 183:5,16 187:21 188:18 188:20 229:15 243:8 245:15 253:12 260:19 260:23 261:9 272:22 273:9 276:10 309:24 310:10,15,20	311:1,9,11,19 312:1,12 315:7 324:10,14,18 328:22 339:11 354:1 355:6 356:18 357:24 360:23 363:2 373:23 378:17 382:8 409:3 446:17 469:13 479:14,19 493:15 498:17 514:6 increases 65:9 89:6 90:9 203:24 447:19 465:4,6 484:14 increasing 254:7 268:20,24 270:11 361:18 435:5 incremental 493:21 independent 47:13 347:1 INDEX 10:2 indicate 125:8 187:18 220:22 242:20 250:5 274:5,10,24 340:17 375:8 407:5 411:15 423:9 431:17 440:7,18 443:3 445:14 452:19 466:4 470:6 indicated 220:19 273:8 273:15 333:13 413:18 428:6 indicates 30:8 30:15 31:15 32:3 40:21 41:2 83:18 93:7 111:19 182:3,22 195:15 202:12	203:20 210:9 224:19 225:1 298:16 325:10 408:12 416:4 420:11 443:19 472:20 487:6 497:8,14 499:3 indicating 84:11 294:2 487:19 indication 466:9 indicative 420:18 436:8 indirect 101:4 indisputable 425:18,23 426:2,6,10 427:8 430:22 individual 19:4 19:7,9 29:5 36:17 194:21 195:8 224:16 225:16,18,19 225:23 227:3 227:24 325:15 375:23 391:2 446:3 469:17 individuals 469:10 induce 174:14 436:14 440:8 440:18 441:7 464:17 466:5 induction 125:5 indulge 457:1 infections 36:12 36:14 inflammation 174:15,18 431:20 434:5 436:14 440:5,9 440:18 441:7 446:17 447:19 448:8 449:3,4 449:16 450:21 451:4,18,21 461:24 464:18 465:2,6,9	inflammatory 487:14 inform 92:17 informal 15:12 information 23:5 48:17 53:9 178:8 277:7 379:14 448:13 463:20 504:4 510:8 informed 156:1 informs 160:1 Ingham 13:6 14:23 38:2 40:23 44:10,14 45:1,12 46:14 46:17,23 47:20 48:1 60:12,23 61:6,22 62:10 64:18 106:2,7 109:20 113:12 116:16 346:11 386:13 515:5 Ingredients 9:22 Inhalation 84:5 inhibitors 461:15 initial 19:24 310:22 initially 306:21 initiation 334:24 initiative 338:18 insanity 227:16 insert 168:9 inside 123:12 instance 435:4 instances 464:7 institution 300:16,21,21 301:5,8 494:9 INSTRUCTI... 518:1 insufficient 510:23 integration 302:23 intend 112:12	112:24 intention 214:4 interaction 38:4 296:13 interest 50:20 53:20 461:7 interested 68:10 205:1 212:5 297:2 390:9 400:15 504:13 interesting 164:12 183:22 228:3 280:19 interestingly 447:7 internal 154:5 154:11,20 478:15 international 79:13 interpret 66:16 66:18 interpretation 277:15 278:5 Interpretations 217:2 interrupt 163:22 190:7 210:1 327:21 357:5 466:23 interrupting 169:8 209:18 209:19 interval 149:24 189:4 193:24 194:8 197:14 202:5,21 203:23 219:8 347:16 348:23 353:18 354:18 370:8 376:24 378:17 386:10 386:13,16 387:3 474:21 intervals 187:5 196:13,23 205:21 217:22
--	---	--	---	--

226:24 235:23	93:3 95:1	44:7,7,18,18	297:5	85:3 86:12
372:8 477:11	131:14 138:13	60:2,2 97:20	jumped 510:21	98:1,9 111:11
intraepithelial	158:19 168:5	97:20 99:8	Justice 495:21	121:22,23
448:20	182:21 234:21	100:22,22	496:5	128:17 129:19
introduction	237:11,20	107:20,20	justification	130:22 134:15
138:9 202:2	247:12 272:7	108:1,1,23,23	267:21	138:10 141:13
382:1 400:14	273:10 321:9	109:4,4,13,13		146:15 149:10
introductions	331:9 355:19	109:21 111:16	K	150:10 155:8
402:24	396:23 426:9	111:16 112:7,7	keep 57:21	155:10,18
invaluable	issued 110:20	112:12,13	166:16,20	156:12 158:14
230:7	111:15 143:19	113:1,1,16,16	167:18 179:14	178:6 199:17
invasive 256:22	494:4 508:9	114:9,9 154:13	183:6 196:14	199:20 200:9
353:17 357:24	issues 26:7 37:2	154:14,22,22	226:17 236:4	205:16 208:13
378:18 451:10	78:7,9,12	315:6,6 354:14	297:16 318:11	209:3,10,21
invested 316:17	116:7 152:5,15	354:14 478:9,9	320:20 321:17	213:20 216:14
investigate	289:18 398:17	478:14,15,15	328:13,14,23	218:11 226:3
316:3 504:1	499:23 507:19	478:16 480:23	417:9,10 423:3	244:8,17,19
investigation	510:14 512:18	480:23 482:11	512:11	247:19,24
154:13	Italy 63:10	482:15,22,23	keeps 36:13	250:22 251:4
investigator's	69:11	483:12,13,23	229:9	255:4 258:10
225:19 227:3	Item 103:16	484:18 485:2	Ken 292:15	258:12 265:14
investigators	146:19	499:5 500:9	Kenneth 199:20	274:20 278:7
224:17 225:16	items 111:8	Johnson's 16:15	286:21 287:8	279:8,20
225:18 227:24	215:22 463:23	16:21 99:8	288:6 292:23	284:18 285:3
invoice 6:9		109:22 482:11	kept 66:22	285:19 288:6
111:15 112:12	J	482:15 483:23	222:13	288:15 292:2,2
invoiced 112:6	J&J 31:3 42:1	484:18 485:2	Kevin 1:13 5:4	297:9,14 298:5
113:19 114:3,8	42:22 47:1,8	499:5 500:10	5:14,17,19	298:7 299:8,14
involve 153:18	J&J's 497:20	journal 6:16 9:8	6:10 11:13,19	299:15 300:1
240:4,7 241:11	JAMES 4:3	115:11 176:22	12:6 110:14,17	302:3,4 304:5
involved 49:22	james.mizgala...	177:2,2,12	517:8 520:16	307:13 322:22
50:8 116:6	4:5	179:4,20	key 47:23 48:16	326:6,8,18
122:1 404:1	January 38:8,9	184:19 200:10	Khabele 461:3	332:20 337:4
479:8	151:4	200:13,17,23	kind 16:10	337:16 338:2
involvement	Jason 488:23	299:20 411:9	knew 284:15	341:15,22
38:3 44:24	489:21	489:24 490:2,9	286:21 506:6	342:19 346:12
46:13	Jersey 1:2 3:9	490:16,22	know 14:21	346:13 350:22
Involving 445:9	3:13	491:1	15:16 18:21,23	362:8,19
irregularities	JNJ 9:7	journals 217:4	20:7 26:21	368:19 375:14
140:11 178:20	job 15:20	judge 168:6	33:23 40:5	382:19 383:23
irrespective	Johnson 1:4,5	169:7	47:9 51:9,22	384:6 386:8,20
235:21	3:15,15 12:21	judgment 156:2	52:7 55:24	389:8 390:13
irritation	12:21 13:1,1	157:10,15,16	61:5 63:6 66:4	390:14 396:22
431:20	16:14,20 32:14	157:20 158:14	66:16,17 67:9	400:18 405:2
isolation 249:10	32:14,24,24	242:18 426:3	73:23 74:9	406:16 417:21
issue 23:14	37:10,11 38:18	Judith 156:17	78:17,24 79:10	427:1,5 439:5
52:15 88:16	38:18 41:15,15	jump 280:6	83:6 84:18	448:14 454:10

459:20 460:11	429:9	leave 258:8	449:18 452:10	243:13
460:13 462:12	late 38:4 335:2	321:24 379:23	473:7 485:19	limitation
466:1 477:10	361:13 369:23	482:7	485:23 494:15	256:15 316:21
480:2,22	473:16 487:10	lecture 24:5	496:23	317:5 344:9,15
489:12 498:7	latency 19:17,23	26:8	letter 9:6 208:21	350:16 351:10
498:11 502:6	20:11,15 21:3	led 49:5 205:14	424:16 426:13	352:6,14
502:15,16,22	21:6,12 325:12	308:3	letters 143:19	367:11 375:18
505:12,14,22	326:5,6,7,11	left 94:10 334:18	letting 167:16	387:1 388:2
505:23 506:10	326:20,21,24	left-hand 181:21	327:9	limitations
507:2,11	327:1,2,3,8	181:23 256:6	level 19:8 97:12	88:15 170:13
509:11 512:8	328:11 331:8	293:4 334:19	189:12,13,15	170:22 308:24
knowledge	331:15,17	486:20	226:6 280:4	309:2,12,15,19
39:14 293:9	332:2,5,16,24	legend 416:4	284:10 307:22	313:17 315:10
498:4	333:14 334:5	LEIGH 2:13	314:4 330:19	315:12,14,24
known 20:1,6,8	334:24 335:19	leigh.odell@b...	330:20,22	351:14,22
262:16 263:3,4	336:2,12,17	2:16	389:14 390:8,9	352:1 353:7
263:6,9,24	337:1,5,7,17	length 345:10	391:20 495:15	404:15 405:20
264:3,16,23,24	337:23 338:11	lesion 448:19	505:19 506:7	406:4,12
265:3,4,8	338:12,14	449:13	514:2	limited 38:21
288:7 335:15	339:14 351:4	lesions 448:23	levels 152:1	39:1,4,8 41:18
knows 67:15	352:16 353:1,1	451:19,22	281:6,10,13	42:1 91:7 95:2
282:16 283:2	353:4 356:8	lesser 323:11	282:14,24	95:19 119:18
331:19 399:11	369:1,11	let's 21:23 39:16	283:11 409:14	128:3 176:2
427:6	laugh 214:6	83:24 102:11	470:20 471:5	235:19 252:16
Kunz 437:19	laughed 214:11	121:13 151:2,3	505:11	389:22,23
	launched 190:18	169:20 173:18	Lheureux 9:16	476:17
L	law 15:11	181:7 182:16	487:4,5	limits 69:24
L 1:15 2:3	lawsuit 264:6	186:3,3 201:15	LHG 1:6	70:10
517:12	lawsuits 265:10	202:13 203:19	liability 1:6	line 10:6,9,12,15
lab 140:12 141:5	276:9 277:14	207:21,21	264:9 266:3	52:18 305:10
141:24 461:8	278:22 279:21	208:3,3 213:18	library 54:17	430:17 513:5
label 501:15	lawyer 81:7	214:12 220:5	lied 178:9	519:4 521:2
labeled 160:23	159:13 199:8	234:23 235:1	lies 371:4	lines 41:11
lack 188:3,14,17	213:22 216:14	250:19 255:12	life 37:2 251:2	45:16 64:23
188:22 238:10	LAWYER'S	270:8 271:6	369:23 444:14	336:1 444:7
307:24	521:1	273:21 292:15	lifetime 250:23	link 306:19
Lancet 486:11	lawyers 56:16	294:23 302:13	417:2 487:8	list 24:8 45:2
Langseth 7:11	107:20	315:22 324:24	ligation 441:23	47:18 49:12,15
271:7	lay 265:14 266:1	334:1 337:12	442:8,17 443:5	49:24 50:3,24
large 139:3	266:2,9 278:15	338:17 343:15	443:20 444:9	51:1,10,23
265:9 316:12	468:7	363:12,12	444:19 446:5	53:7 54:4,17
317:10 328:21	lead 274:5,11,24	377:19 383:12	light 399:14	55:12,20 56:3
506:10	leads 188:23	389:2 406:18	likelihood 17:16	56:15,18 57:14
largely 149:4	464:18	415:14 416:14	17:20 352:24	69:21 106:20
227:5 321:11	learn 388:22	416:14,17	likewise 125:3	110:23 119:14
410:9	503:22	418:12 420:6	limit 48:15	121:2,11 124:2
larger 202:17	learned 284:5	421:13 440:4	225:9 243:12	131:13 138:17

139:17 142:1	181:14 182:4	338:10 431:11	330:1,6 334:8	233:24 236:21
142:12 143:2,6	185:13 206:16	453:8	350:5 356:2	238:2 281:23
148:21 149:1	206:20 210:19	long-term 384:7	357:11 362:23	281:24 284:4
149:21 150:6	220:21 241:5	417:2	365:17 377:3,4	289:7,10
152:4 155:12	246:15,21	longer 311:4	377:20 388:18	315:23 317:9
231:23 233:11	247:15 248:23	355:23 361:17	395:24 396:1	374:23 375:4
233:14 235:16	253:10,15	373:3,18,22	397:10 415:14	375:11 377:2
293:13 388:24	262:4 289:12	382:9 385:11	416:14,14	410:9 415:19
424:19 441:2	307:20 313:7	495:13	420:6 434:14	415:20 416:2
441:15 463:23	336:21 352:7	Longo 478:10	434:23 435:10	429:17 430:1
507:12	359:17 389:12	Longo's 170:7	436:2 447:8	454:8 473:1
listed 49:12 53:3	390:12 470:24	look 31:21 39:16	449:22 450:10	475:11 477:5
111:3,7 117:2	483:1,15,21	53:11 72:5,7	450:13 451:9	504:13 505:3
117:21 119:13	509:6 514:23	72:11,17 73:6	460:13 471:23	looks 67:10
143:1 146:3	lithotomy	75:3,3,11	474:17 475:1,8	125:12 228:20
167:5 405:22	438:20	78:13 87:12	477:23,23	232:6 321:24
408:9 489:5	litigation 1:7,20	88:18,21 93:5	485:16,20	448:14 511:10
listener 468:7	11:5,11 12:20	129:10 130:1,5	486:21 492:11	loosely 149:17
listening 300:14	37:11,12,24	130:15 135:14	496:14	losing 94:20
332:13,14	43:4 103:18	136:7 141:16	looked 57:1,4,11	lost 348:9
listing 24:6	108:6 113:18	142:1 143:6	77:18 115:19	lot 77:8 169:21
lists 49:13 51:15	115:5,7,10	146:19 149:14	115:22 116:4,5	233:17 279:15
52:24 57:12	154:8 266:10	164:13 165:6	129:21 134:22	322:10 355:19
58:19 74:7	396:19 479:9	178:20 181:7,9	137:5,8,13	392:4 403:10
105:6 112:1	505:2 515:14	181:17 182:16	142:7 149:20	448:23,24
117:3,22 146:4	little 24:3 35:10	189:9 192:8	149:21 151:19	471:1 493:18
146:14 304:4	42:14 57:22	201:15 202:23	151:22 165:21	499:22
305:8 381:10	61:9 82:22	208:19 210:7	206:17 236:18	loud 297:12
497:16	84:19 85:5	220:5 222:14	237:2,11,20	louder 57:22
literally 472:11	230:13 240:22	231:21,23,24	238:8 320:22	love 297:5
literature 43:13	305:13 321:13	233:17,18	321:11 323:12	low 185:22
43:16 47:24	365:2 415:4	236:7,16 238:8	323:18 352:6	245:21 307:22
52:2 57:9,11	438:21 445:20	255:12 256:10	359:18 418:4	325:20 329:17
62:5,7 67:9	502:22	256:10 262:14	420:23,24	330:19,22
90:20 91:3,23	lives 352:11	266:13 269:12	448:12 452:12	387:22 460:19
92:20 97:18	living 251:10,11	269:13,22,24	461:9 493:20	461:18
104:21 105:10	LLC 4:6,6	270:8 271:6,17	495:6	lower 435:15
105:21 106:13	LLP 1:14 2:7	271:18 282:7	looking 73:8	lowest 248:11
111:20 116:20	3:3,7,12,17 4:2	283:22,24	97:16 116:7	LPA 151:23
128:6 131:17	long 26:21 35:4	285:4 288:19	120:10,13,17	ludicrous
133:2,5,22,24	112:20 226:17	292:15 293:3	122:9 123:8	203:21
134:2 136:24	284:7 293:15	300:15 301:23	127:7 128:7	lump 373:12
137:5 146:15	313:22 325:12	303:15 307:18	137:10 166:15	lunch 125:13
155:18 157:11	326:5,21,24	313:6 315:22	166:18 181:16	223:23 239:17
157:14 162:10	332:23 333:8	318:17 319:13	197:10,11	239:23
162:14 165:7	334:23 335:19	322:3 324:6,24	200:5 202:2	lung 306:20
173:24 174:12	337:5,7,17	326:12,15	227:5,14	342:4 468:20

lymph 123:9,12	management	224:5 255:14	396:14,17	345:9
lysophosphati...	281:17 303:10	258:21 271:10	423:3 492:23	mechanism
151:24	305:20	273:23 292:17	513:8	57:17 58:6
M	Manges 1:14	302:9 333:21	matters 13:23	65:12 126:22
M 2:13 3:3,8,12	3:12	344:3 363:14	14:13 396:18	140:6 142:8
426:24	manifestation	377:12,15	McCLENNEN	174:1,13 393:6
M.D 1:13 2:13	335:1	403:21 406:21	3:3	394:6 401:7,24
5:4 6:10 11:19	manner 168:13	407:17 424:10	MD 5:15,17,20	422:1,19
147:2,19	mantle 372:24	428:15 468:2	MDL 37:24 43:3	423:13 427:16
488:24 517:8	manufacturers	471:7 486:12	43:9 44:8	436:13 439:22
520:16	154:21	488:10 496:19	59:10 60:2	440:8 441:6,20
ma'am 75:5	manuscript	503:1	104:11 105:24	445:5
159:15 206:13	118:9,22	market 500:17	115:1,6 515:7	mechanisms
207:19 354:21	March 1:10 11:6	501:16	515:15	423:2 432:11
425:11 473:5	111:15 147:20	MARKETING	mean 17:6 33:18	mechanistic
macroscopically	151:5 200:7,8	1:5	37:3 39:1	57:3 492:18
450:7	486:11 503:11	marking 378:5	40:16 47:10	media 266:1,2,9
magnitude	517:15	marks 516:3	59:9 70:4	277:8 278:15
246:4,13,19	MARGARET	Marte 4:10 11:4	76:19 78:8,10	medical 12:8,18
247:9,10,20	2:13	mask 63:8	118:8 121:10	13:14,24 17:23
main 448:5	Margaret.tho...	369:14	132:2,24	18:9,13 23:6
majority 128:18	2:15	masks 69:8 78:1	178:11 179:23	33:4,12,16,18
234:5,5,6,10	mark 39:18,19	332:17	196:6 205:21	34:22 35:11,24
234:13,13	40:6 45:9	mass 151:21	234:19 255:3	36:6,16 37:6
235:24 240:15	64:12 71:8	Massachusetts	257:17 264:1	156:2 173:10
265:19	102:11 110:8	3:4 226:9	283:1,1 284:3	185:10 272:20
makeup 496:4	114:24 148:15	material 47:12	299:21 340:6	281:19 283:10
making 67:2	154:22 180:8	materials 6:8	364:14 395:22	283:11,23
69:8 77:24	186:5 200:3	23:3,14 45:19	400:6 433:15	284:12 301:3
81:16 120:12	220:10 224:3	45:20 47:7	438:5 450:7,9	301:11,12
196:15 205:9	255:18 274:3	51:14,17 52:7	472:1,10	303:19 372:5
278:24 299:22	292:21 302:13	53:1 110:16,19	498:21	medical/legal
319:24 332:17	334:1 344:1	117:19 121:11	meaning 85:19	499:23 513:6
341:2 423:22	363:18 377:19	146:21 155:15	195:16	medication
425:22 435:11	403:19 407:1	189:6 194:4,22	means 33:24	33:23 34:5
437:14	407:21 424:14	279:5 384:2	34:3 78:1 86:6	35:14 36:21
malignancy	471:11 486:9	math 234:8	177:9 184:16	medications
25:13,22	488:9 496:23	350:10,12	205:23,24	33:2 36:24
455:20 466:16	503:5	matter 11:10	217:5 312:20	37:3,4,7
467:13,18,20	marked 10:14	13:6,20 14:5	398:9 517:20	medicine 7:19
469:17	40:12 45:5	14:17,23 45:13	meant 233:20	7:19 9:9 178:2
malignant 19:11	64:13 71:4	46:23 49:12	measure 262:1	205:13 235:24
25:6 79:11,20	102:13,17	51:11 64:18	measurement	281:15 302:18
336:3 466:10	110:4 114:20	69:21 104:1,10	262:5	302:22 303:5
469:14	121:8 148:9	106:2,14	measures	303:17,20
man 456:5	180:4 186:6	107:13 108:11	217:23	305:20 306:1,5
	199:23 220:14	109:20 148:23	measuring	394:17 446:20

Medline 119:22	449:7	285:2,10 289:6	388:3 404:5	338:9
meet 246:3	mentions 149:4	289:10,13	416:6 417:11	misconceptions
247:11	238:5 323:15	290:10 291:3	mic 469:24	7:17 292:23
Melissa 242:8	mere 393:22	308:17 312:7	Michelle 1:15	293:14,17
member 176:17	394:18,24	318:13,22	517:12	294:15
507:3	400:21	319:22 321:18	microphones	misdiagnosed
memorable	Merritt 265:17	322:4,5,7	126:10	93:10,16
250:7,9 251:12	mesothelioma	329:21 360:4	microscopically	misdiagnosis
251:19 257:2	78:23 79:12,14	360:12 361:1,7	449:24 450:9	86:22
257:10 258:4	79:21 86:23	412:4 413:10	middle 214:15	misinform
267:23	93:10,17	413:14 420:12	334:21 351:13	203:5
memory 48:9	469:14	443:4 444:2,17	374:13 375:1	mislead 204:6
123:9 263:2	message 125:17	446:2 453:15	416:19 424:23	misrepresented
266:20 280:5	met 477:9	455:4 474:7	425:3,9 497:14	154:14
347:1 419:23	meta 232:14	476:13 493:17	migrate 130:17	missing 204:23
menarche	meta-analyses	Metal-Analysis	131:18 135:17	339:14
487:10,10	8:21 206:23	8:18	138:5 174:2	misspoke
menopausal	220:20 221:3	metals 5:22	422:3 425:16	403:16
245:2	221:11,19,24	71:10 109:5	427:17 430:19	misstated
menopause	222:3,22	170:9	431:18 436:14	371:13 461:11
243:16	223:11 224:4	method 163:5	439:23 441:21	misstatement
menses 173:12	230:8 231:18	methodical	442:7,15	158:16,17
mental 118:16	233:5,6,7	163:6	migration 116:7	misstatements
mention 31:23	241:4 270:19	Methodological	121:16 122:11	489:18
101:17 134:12	270:20 284:16	271:20,23	129:9,22	mistake 77:10
135:8,11 138:3	284:19,23	methodology	130:12 131:15	196:15 279:19
141:4 164:2	285:13 287:19	115:19,21	133:3,22 134:9	379:23 380:12
172:4 237:1	287:22 288:18	159:23,24	134:20 426:9	383:2 412:1
323:15,17,19	292:8 304:22	160:2,11,13,15	428:7	413:19 414:3,5
329:9 357:12	305:1 307:2	160:17,24	Mills 7:8 255:19	414:8,11,14
379:13	309:20 311:10	161:4,11,13,17	mind 55:17	mistaken 190:21
mentioned	311:14 315:14	162:3 163:4,9	263:12	mistakenly
88:16 114:12	319:17 406:19	172:15,20,21	minute 86:21	217:5
120:3 130:6	407:6,7 408:7	173:1 195:1	363:8 397:11	mistakes 78:8
134:19 135:1	408:10 409:15	288:8 495:7,9	462:21	279:14 319:24
136:10 137:22	409:22 410:18	methods 161:20	mischaracteri...	383:1
138:22 171:23	419:4,12	189:7,8 194:4	464:11	misunderstan...
235:16 333:11	492:13,14	194:22 279:6	misclassificati...	193:15 276:21
352:15 353:10	meta-analysis	293:10 384:2	61:3 78:12	misunderstood
358:21 397:2	6:21 9:14	404:10 475:8	87:1 93:3	451:8
417:7 447:17	145:18 146:2	504:9	94:16	misuse 217:19
449:19 455:6	225:22 227:7	metric 261:24	misclassified	mix 290:21
461:2	229:8 230:15	262:1,18	93:19,24	291:18 311:16
mentioning 24:9	230:16,17	263:10,21	misconception	311:20 320:17
70:21 133:1	232:11 236:8,9	267:13 343:4	294:3,11	mixed 237:5
300:11 352:13	236:12 270:18	344:16 368:1,5	296:23 298:16	319:15
352:22 382:10	284:20,22	368:7 376:3	298:19 300:5	mixes 398:20

mixing 69:10 289:15	75:14 76:1,9 76:10,12,23,24	Musser 9:6 426:20 427:1	210:12 211:22 215:7 226:16	450:12 488:16 498:8,12
MIZGALA 4:3 30:19 32:7	82:6,8,10 83:8 84:21 85:14,15	428:9 mutation 455:22	232:24 258:10 258:12 318:15	503:19 505:14 509:15 514:4
168:8 211:3,15 213:3 240:21	85:21 86:15 87:5 88:15	<hr/> N <hr/>	329:16 365:15 366:12 385:24	Newport 2:4 news 185:7
241:1 295:17 439:11	100:19,21 129:15 130:8	N 5:2 naked 270:13	386:2 399:14 480:2,22	newspaper 185:8
Mm-hmm 61:11 102:24 105:13	247:21 Monographs	name 11:3 12:5 12:6 14:4,7,8	needs 125:19 194:15	NHS 378:9 NHSI 367:5
200:15 207:17 223:20 250:10	5:21 Montgomery	41:7 287:21 490:2,10	negate 362:17 negative 24:11	NHSII 367:1,4 Ni 453:18
304:23 342:22 343:2 366:12	2:14 months 404:8,17	napkins 354:1 Narod 6:14	183:4,17 184:2 184:7,14 186:1	nice 196:6 nickel 109:5
367:10 386:17 408:8 425:2	morning 12:2,3 mortality 87:21	180:13 185:16 249:3 259:8	189:21 197:22 197:23 198:4,6	nine 376:10 492:14
mode 323:12 447:2	Motion 67:19 76:16 80:14	260:6 261:18 267:18 318:9	198:12 371:10 371:12,18,21	no-no 320:5 node 123:12
model 129:4,12 129:12,13	144:8 163:15 206:5 356:14	318:15 329:7 329:14,24	372:12,14 381:15 443:4	nodes 123:9 non-aspirin
132:13 136:1 296:11,11	430:23 446:8 456:19	330:14 346:3 385:24	444:18 447:10 neither 203:1	454:1 non-diseased
models 130:11 131:9	move 54:15 95:9 141:14 162:7	Narod's 260:6 263:16 329:10	391:10 416:11 Ness 440:23	390:22 non-exposed
moderate 222:9 modest 247:2,16	213:18 214:12 214:14 297:23	narrower 61:10 National 446:19	441:4 never 22:1,7,12	398:1 non-perineal
271:3 357:23 484:9	300:13 401:1 415:6 418:10	nature 14:17 20:17 24:18	23:21 24:21 77:18 128:24	417:1 non-persuasive
moist 36:12 molecular 124:8	418:13 movement	122:3 148:5 190:17 200:8	132:12 139:4 178:17,18	128:5 134:6 non-significan...
432:11,19 433:10,17	173:13 moving 495:12	200:14 205:10 226:16 250:14	197:16 198:21 202:14 238:9	215:21 217:5 236:3
435:2 molecule 394:19	mucinous 324:16,20	301:22 396:19 near 210:21	259:5 282:15 282:16 283:1,2	non-statistical 202:4
moment 43:16 120:17 515:18	409:5 multi-discipli...	nearly 458:8 necessarily	287:18 289:3 341:23 344:24	non-statistically 216:5
money 113:11 316:16	450:12 multi-district	123:2 299:11 306:9	368:3 373:8,14 423:24 437:15	nonconsistent 183:5
monies 145:13 monitor 504:1	37:12 multiple 66:19	necessary 44:2 392:12 518:4	449:14 451:17 459:3	nonmalignant 9:11 467:24
monitors 118:21 monograph	277:9 278:12 multitask	neck 513:11 need 81:3	nevertheless 20:14	468:6,16,18 469:11
60:24 61:18 62:9 63:5	332:13 multivariant	110:22 125:9 151:6 156:12	new 1:2,14,15 3:9,13 9:17	nonresponsive 67:19 144:9
68:21 69:17,24 70:10 71:9	348:1,22 multivariate	159:11 165:8 190:1,13 205:4	11:10,10 14:11 169:14 227:9	206:5 356:14 418:22 430:24
72:4 74:22	354:21	205:6 209:3,9	228:2 301:6,17	446:8 456:20

nonsignificance	73:15 74:16	object 24:1	173:4,14 174:4	318:5 319:8
204:20	82:5 105:4	26:23 27:13	175:21 176:4,9	327:12 330:7
nonsignificant	138:8 140:11	28:3 29:2,20	177:4,18 179:5	331:11 333:1
183:17 201:22	146:23 147:6	30:19 32:17	185:2 188:4	335:7 338:6
203:22 205:14	147:14,18	33:13 34:17,24	192:3,17	340:20 341:8
210:12 270:2	181:13 182:3	35:15 36:1	193:12 195:5	342:10 343:8
nonstatistically	229:7,11	38:22 39:5	196:18 197:4	343:12 344:19
204:17 296:18	230:21 251:23	42:3 43:22	198:13 202:7	345:11 346:5
298:20	293:18,20	44:19 46:2	203:13 204:12	346:16 349:5
nonsteroidal	296:8 316:12	47:2 48:7	207:1,12 211:3	349:20 355:12
455:11 459:17	317:23 328:5	49:17 50:14	211:5,15 213:3	356:20 358:11
nonsteroidals	329:17 330:2	51:2,19 53:4	213:5 215:3,9	359:1,10
460:12	361:22 384:20	55:22 56:11	216:6 218:4	360:16 362:10
normal 442:16	386:9 387:3,9	57:19 58:8	219:10 221:6	364:13 365:8
normally 154:20	387:19 410:3	60:5,16 61:24	221:21 223:4	366:6 369:7
NOS 435:4	466:8 487:8	62:17,24 63:21	225:3 230:10	370:18 372:20
Notary 1:17	493:17 497:16	65:16 70:12	231:4 232:15	375:20 379:20
517:14 520:23	numbers 9:7	77:4 84:14	234:16 235:7	381:7 382:23
note 350:16	93:18 198:22	89:21 90:22	235:13 237:24	385:6,19 386:6
351:13,17	207:10 260:17	91:24 95:4,20	238:20 241:13	387:5,15 388:6
416:22 417:14	290:6 331:2	96:12 98:8	242:2,13 244:1	388:14 391:7
notebooks	471:17	99:21 101:20	244:14 245:8	393:7 394:8,14
141:24	nurses 366:1,2	102:7 103:19	245:22 246:7	395:15 397:15
noted 11:14	Nurses' 256:18	104:13,23	246:22 248:3	398:3,23
87:18 141:24	311:8 344:10	106:8 108:12	249:7,22	399:19 400:3
518:11 520:11	363:22 365:21	109:7,15	250:11 251:14	401:9 402:2,10
notes 106:5,15	365:23 376:21	112:15 113:22	252:12 253:2	406:1 408:17
118:6,15,16	378:9 380:21	116:21 117:7	253:21 254:9	410:21 412:13
119:1,10	381:4,20	117:23 118:18	257:12,21	412:21 413:21
140:12 141:5	Nutrition 427:4	119:5 121:9	259:24 262:8	414:19 417:16
485:21 521:1	428:12	122:6,16	265:5 267:8	419:8,21
notice 1:14 6:6	NUTTER 3:3	124:11 127:20	268:13 272:24	423:17 427:19
102:11,18	NW 3:18	130:20 131:23	277:18 278:16	431:8 432:21
noting 351:9		136:13 137:2	279:2 282:11	433:6 434:1,19
notion 296:16	O	139:23 142:3	282:11 283:13	435:6 436:16
November 38:5	O'DELL 2:13	142:16 143:3	286:16 287:24	438:2 439:9,11
38:6 43:6	80:22 81:11	146:6 147:5,11	288:9,23	440:11 441:11
NSAID 448:1	167:19 169:10	150:17 152:7	289:21 291:4	441:24 442:10
452:11 454:2	208:7,12,17	153:8 155:2	295:15,17	447:4 448:3
456:1,15	458:17 462:13	156:3,14	296:2,20	451:5 452:21
NSAIDs 452:11	462:19,24	157:17 159:1	298:24 300:18	454:21 459:10
452:13 455:16	463:13 464:3,6	159:17 160:20	302:1 303:12	460:3 462:5
455:23 457:11	464:13	161:7,24	304:14 305:16	464:20 468:8
459:7,7 460:16	O'REARDON	162:19,24	305:22 307:7	469:2 470:15
461:16	2:7	165:11 166:2,9	312:2,15	473:14 475:23
NTP 485:17	oath 11:17 15:7	170:16 171:12	315:15 316:6	477:20 480:5
number 73:13	15:9	172:1,7,17	316:22 317:18	481:2 482:18

484:19 485:4	occasions 464:8	15:24 16:11	321:19 324:22	oncology 39:10
487:22 489:9	occupation	21:15,24 32:24	328:19 334:18	176:18,22
491:5,17	27:11	42:20 72:8	334:20 337:21	178:4,14 179:3
492:24 494:11	occupational	74:3 75:5,10	337:22 342:1	179:23 180:11
496:7,16	27:17 28:6	75:13 77:2	343:15,17,21	181:4 249:15
497:23 499:8	60:13 61:13,16	83:15,24 87:2	345:16 348:14	456:11,14
500:2,13,21	61:22 62:15,22	87:11,12,17	350:7,11,14	507:6
501:8 504:16	63:3,17 64:3,9	89:15 96:21	351:24 354:22	one-sided 388:3
505:6 506:21	65:5 67:7 68:1	107:9 111:13	355:4 363:6,9	one-time 366:21
507:23 508:16	68:19,20 70:1	119:1 126:8,14	365:4 366:17	367:3
509:23 510:18	70:11,18 71:1	127:16 129:18	366:17 367:13	ones 15:4 55:13
512:3,22	80:5 86:5	134:24 138:22	368:11 371:16	78:11 117:11
513:12 514:10	87:22 88:8	143:1,18	372:15 374:8	152:24 259:23
514:16	95:13 98:15	144:24 147:22	375:13 377:3	270:9 312:21
objecting 30:23	326:16 330:10	150:21 155:11	377:19 378:2	312:23 325:24
objection 16:23	331:23 332:7	156:23 159:21	383:4,12,22	409:3 509:10
17:12 18:1,11	335:17	165:17 171:5	384:5 386:3	509:11
19:1,19 20:19	occupations	172:13 173:23	388:2 391:1	onus 205:7
25:15 26:2	26:18	176:16 180:1	396:10 400:24	262:19
27:3 31:5 32:7	occur 65:13	180:20 181:7	402:8 403:4	op 185:9,11,12
33:7 66:5,5	133:4,6,23	181:23,24	404:22 409:12	200:24 329:10
67:18 70:4	occurred 240:8	188:24 191:1	416:3,16	489:20
124:23 131:20	odds 192:14,21	192:8,22	418:12 420:6	open 14:18
190:24 206:4	206:21 241:23	197:21 199:17	421:15 433:1	107:7 173:11
213:16 233:1	243:23 244:8	207:8,21	436:4 438:13	299:20 420:8
341:4 356:13	244:11,17,22	212:19 213:11	449:18 452:10	423:1
364:5 418:21	245:21 253:12	214:1,14	453:3,5 454:9	open-ended
446:7 456:18	269:13,22	215:14 216:16	469:6 475:18	139:7
456:19 466:22	270:10 271:1	216:19 218:23	476:12 477:1	opening 100:18
objections 65:21	311:22 325:20	220:7 222:1	482:8 484:3	operate 259:15
68:5 81:2,16	329:17 354:16	223:24 227:21	485:19 486:1	Operation
103:5 107:16	371:18 378:14	231:14 235:19	486:24 487:2	428:11
objective 262:1	408:13 443:23	240:12 241:18	503:18 515:12	operations
262:5	offense 40:18	243:4,10,15	515:17,19,24	427:3
observations	offer 44:2	245:14 246:12	516:2	opinion 21:3
475:4	138:12 212:8	253:7,16	old 229:9 372:7	43:12 44:2,14
observed 93:12	offered 60:24	255:12 256:13	omitted 127:17	44:22 46:11,16
204:3	308:4	258:2 259:3	once 63:2	47:13,15,20
obstetrics	oh 72:9 83:13	268:9 270:14	193:24 198:10	48:1,17 49:6
488:15 490:1,1	135:6 151:13	274:21 279:17	276:1 332:12	60:13,21 61:12
490:11	153:2 175:13	282:23 287:4	368:1,2 370:6	61:15 62:4,21
obtained 119:17	180:9 219:18	287:18 296:6	389:7 495:24	63:3 64:7 69:6
obvious 370:22	250:24 377:13	298:5 301:4,18	oncologist 12:11	69:15 70:15,22
423:1	378:2 415:20	302:8 304:3	12:14 126:20	78:18 86:12
obviously 213:8	429:24 441:13	306:13 308:20	176:17 242:10	89:23 91:19
372:2	465:12 487:2	309:7 310:13	oncologists	94:23 95:10
occasion 243:17	okay 15:4,5,23	312:10 317:3,8	136:22	97:3,4 99:5

100:1,2 108:20	52:3,9 68:18	outcomes	138:2 145:8,14	405:16 408:6
108:22 109:2,3	69:3 90:1	316:13 417:6	149:8 151:11	409:21 410:19
109:10,12,18	92:18 95:19	outlined 251:24	151:18,22	410:20 413:12
109:21,24	107:22 108:2,4	outmoded	153:5 165:3,23	419:6,18
116:9 162:18	108:10,17	293:12	174:15,20,23	420:16 425:14
164:4,22	115:14 117:17	outside 19:9	175:7,16,20	431:19 432:9
165:10,15,16	117:20 123:15	46:6 62:4	176:8 180:12	432:12,20
171:8,19	123:21 138:17	66:23 67:3	182:2,9 189:19	433:11 434:6
173:23 174:7	146:17 155:13	69:14 80:4	206:8,12	443:24 444:20
174:11,21	155:20,23	86:8 98:14	220:24 224:21	446:18 447:12
175:3,5,8,14	156:1,13 157:3	100:11 446:1	241:6 243:11	447:20,24
175:17,18,24	160:3 161:5,17	outstanding	245:6,16	448:2 449:9
176:2 188:7,11	172:14,16	14:3	246:15,20	450:5,14
188:15 191:14	173:3,19	ovarian 6:13,23	248:12 249:19	451:14 452:7
191:19,22	211:20,22	7:7,10,13,22	252:10,17	452:16,20
199:3,5 200:12	212:2,5,10	8:7,9,12,15,17	253:19 254:5,8	453:17,23
203:11 211:14	253:14 271:8	8:20 9:13,15	256:15,22	454:2,13,19
230:4,9 235:12	304:12 307:6	9:18 13:2,11	265:11 266:17	455:5,14,24
241:21 242:6	426:5 491:15	14:14 17:11	267:5 276:15	456:16 459:24
246:10,13,18	492:22 497:22	18:19 19:18,22	278:14 280:17	461:23 462:3
247:8,18	499:7	21:4,16,17,20	310:2,21	464:18 470:7
249:13,17	opportunity	21:20,21 22:8	311:12,23	476:16 479:15
252:20 260:6	146:15 159:13	22:13 23:1,4	312:1 316:5	479:23 480:16
261:18 263:16	216:21 297:8	23:10,21 24:23	317:9 324:11	481:24 482:6
265:4 267:17	298:10 517:9	25:4,8,10 28:9	325:13,18	484:15 487:1,7
268:9,21	opposed 113:8	28:19,22 30:9	326:5,6,11,13	487:13,21
285:21 286:4	197:8,12 329:8	30:16 31:16	326:16 327:1	488:17 501:3
288:22 308:4	467:19	32:4,13 37:23	327:10 331:8	508:11 515:9
309:22 310:9	opposite 50:17	43:14 44:4,16	331:16,18	ovaries 65:9
312:11 315:8	88:22 91:17	44:23 46:12	332:23 334:11	130:18 131:22
318:8 327:4,7	247:8 423:11	56:24 60:15	334:23 336:3	132:8,19 134:3
327:22 328:10	optimal 388:12	61:14,20,23	336:19,23	138:11 174:3
329:11 332:4	388:18	62:16,23 63:14	337:4,15,17	390:1,2,3
360:9 371:21	options 475:12	63:18 65:1,6	340:1 347:5	391:5,13 422:4
395:11 401:20	Oral 6:6	65:10 67:23	351:5 353:17	422:22 423:16
419:5,20	order 45:21	69:12 70:1,11	354:17,22,24	426:1 427:18
421:24 422:5	154:24 270:7	70:19 71:2	355:7,10,11	432:1 438:17
422:22 441:18	458:12	77:15 78:21	356:19 357:9	439:4,23
441:19 442:6	organ 394:20	79:19 86:22	357:17 358:1	441:22 442:8
447:18,23	organization	88:24 89:4,6	367:7,8,16	442:15 445:11
448:6 452:6	494:10 507:9	90:2,4,7,9,14	369:2,5 370:7	445:24
464:17 472:13	509:20	90:21 91:7	372:11 374:17	ovary 87:20
479:13 494:4,7	original 91:18	93:11 95:15	378:12,13,18	89:20 95:12
513:15	217:16 423:21	98:18 100:5	378:20 380:3	128:11 130:4
opinions 37:17	518:15	101:17 113:18	385:13 386:1,4	390:15 396:21
37:18 44:9	outcome 227:16	116:10 120:7,8	390:21 393:4	400:22
45:21 49:11	412:12 417:4	120:9 124:10	394:5 405:9,12	overall 311:6

378:10 392:5 479:21 overcome 314:7 overconfident 217:13 overlap 56:5 230:18 231:21 233:17 234:3 234:14,22 235:5,12,17 236:2 321:12 322:10 323:23 409:15 410:3 oversimplifying 99:23 overstate 395:5 Ovulation 7:21 ovulations 487:8 owned 301:16 oxygen 435:12 435:20 oxytocin 128:16 438:21	72:4,21 74:2,5 76:23 82:5,13 83:5 84:16,18 84:23 87:5 93:5 116:12 125:8 126:18 127:4,7 133:15 134:8,9 135:7 140:9 141:8 160:9 181:10 181:11,21 182:20 187:18 202:20 217:1 217:10 224:11 224:13 256:4,6 258:23 261:5 271:14,15 274:4,8,10 275:13 281:1 325:4,5 334:3 334:16,20,21 350:15 357:14 358:2 365:20 367:24 374:13 374:14,18,19 375:2,6 377:5 384:19 407:8 407:10,14 415:15,22 416:17 420:10 424:23,23 425:2 429:17 429:18 430:3 430:13,13 442:23 443:1 443:17 446:11 471:16 476:9 478:4 519:4 521:2 pages 48:11 71:23 428:18 430:6 471:19 520:6 paid 112:9 113:11,19 114:4 paper 50:21,22	55:9 58:21 73:13 121:15 121:16 122:4,8 122:15 123:14 123:20 124:7 134:13 151:3 171:11 180:2 180:10,15 181:1,5 182:17 184:10 185:7 194:21,23 195:14 200:4,6 200:6 201:16 202:1 203:16 207:22 213:9 215:8 219:4,9 219:17 223:15 255:1,19 256:5 263:17 271:6,7 271:22 273:22 275:4,14 285:20 287:10 292:15,22,24 295:1,6 298:15 318:9 323:7,21 323:23 325:7 329:14 347:2 350:18 394:1,2 397:7,11 398:16,16 400:14 407:2,4 409:22,23,23 411:8 416:18 417:19 421:9 428:6 432:3,18 433:2 434:13 434:22 435:9 435:24 437:20 441:9 443:8,10 443:12,16 446:21 447:9 447:10,11 459:23 462:2,8 468:23 471:12 471:16 486:10 486:17 493:4 495:11 498:18	papers 49:23 53:2,24 55:2 56:19,23 57:2 57:5 61:17 62:8 88:18 91:12 111:7 118:23 138:8 139:13 140:4 149:6 152:18 258:18 261:21 267:4 297:10 352:8 489:22 498:19 paraffin 400:1 paragraph 74:21 87:14 127:8 256:7 258:24 275:16 325:6 379:3 380:13 407:14 416:19 443:19 469:7 paragraphs 139:4 166:19 456:23 457:15 457:20 458:9 465:20 Pardon 156:9 468:13 Park 3:9 part 51:5 68:11 77:2 78:17 81:19 87:3 107:2 143:8,13 143:14 146:8 153:16,20 158:13 251:5 251:10 271:8 284:10,12 289:6 304:13 327:16 384:16 393:13 427:14 429:9 448:21 participants 240:4 330:3 387:4,10,11,12 participated	63:7 particle 393:23 394:19 particles 122:12 123:11,11 127:24 128:10 128:14 133:3 133:23 134:10 391:11,24 392:2 400:22 430:18 431:17 437:3 particular 31:23 135:18 156:24 490:13 particularly 23:8 particulate 135:15,18,20 423:3 438:14 particulates 425:16 partners 242:9 504:7 parts/genital 376:6 pass 39:21 passage 173:12 path 449:24 pathologic 78:14 94:7 pathology 94:11 94:13 449:22 patient 14:8 19:4 26:9 27:2 28:11 35:23 36:7 128:16 338:10 450:12 450:14 479:4 479:20 480:21 482:13 483:11 483:24 485:9 501:2,5 502:12 506:19 511:15 patient's 14:7 26:14 patients 9:11
--	--	--	---	--

25:2,6,21	pelvis 430:19	percent 25:5,9	344:24 347:4	202:12
26:17 27:7	431:19	25:10,11,21	353:24 367:15	ph 1:20
225:24 233:23	penalty 15:7	149:23 187:4	422:3,21	Ph.D 427:1
239:1,5 244:23	pending 168:22	187:21 193:21	423:15 425:16	428:9
272:17 313:22	210:2 418:17	193:23 194:8	427:18 439:3	Ph.Ds 153:19
342:3 356:12	419:1 454:5	196:22 197:14	445:22,23	pharmaceutic...
367:7 405:14	Penninkilampi	202:5 205:20	period 19:17,23	84:3
418:4,20	8:19 171:10,20	234:2,4 235:5	20:11,15 21:3	phase 452:3
455:21,23	171:24 227:9	245:15 248:19	21:6 261:22	phenotype
466:12,16,17	229:23 230:1	248:20,24	266:15,15	19:12
467:8,12,17,19	231:20 233:9	249:6 290:14	325:13 328:11	phrase 19:17
467:24 469:14	234:7 236:16	318:21 328:22	332:3,5,17	20:6 358:18
483:6 499:13	236:17 237:10	329:2 349:12	334:24 336:2	407:12
500:11,24	237:19 238:7	349:13 371:3,3	336:17 337:7	physically 105:9
501:17 506:9	319:5,11	372:8 376:23	337:23 345:19	105:12
506:12 507:21	320:21 321:10	378:16,16,20	350:2,4,6,15	physician 307:1
508:14 509:1	322:3,12,15,19	386:23	351:3 352:14	pick 151:21
510:2,7,16	322:21 323:4	percentage 25:1	369:3	279:10 281:21
512:16 513:1	360:4 361:13	150:2 234:9	periods 21:12	313:3 314:9
513:11,20	362:7 382:16	235:11 323:12	325:14	352:16 388:20
514:5	383:5 407:2,4	381:13,14	peristalsis	picking 84:18
patients' 303:1	409:4,23 411:8	perception 35:5	437:21,24	231:10 329:3
PAULA 2:8	411:17 412:2	perfect 388:9	peritoneal 79:20	picture 307:19
pause 132:11	415:15 416:15	504:11	86:23 93:9,17	piece 68:8
348:13 382:6	416:18 417:9	perfectly 380:16	423:4 425:17	200:24 261:18
453:11 473:12	459:23 460:9	475:7	perjury 15:8	489:21
pay 60:9	461:11 471:4	perform 153:21	persist 293:15	pieces 48:16
payments 265:9	488:6 489:4	performance	Persistent 7:16	pig 129:12
Pbrown@bho...	494:14	14:19 20:12	292:22	pigs 130:10,10
2:10	Penninkilamp...	performed	person 30:23	pipes 266:2
PCPC 3:20	230:15	149:3 249:20	34:7 41:5	piqued 50:20
peer 299:16	people 32:20	412:4 413:9,14	81:15 90:12	53:20 461:6
382:13,17,20	35:5 81:9	444:9,13	158:9 178:22	piquing 48:9
383:5 470:18	100:14 149:10	perineal 6:22	179:15 195:8	Pisano 168:6
peer-reviewed	214:19 215:21	7:6,9 8:12,17	399:8,9	place 28:23 29:9
184:10,19,24	235:24 254:16	84:7 120:8	person's 157:14	29:13 128:14
220:21 247:7	262:22 265:14	134:2 220:24	157:16	217:24 218:7,8
254:3 257:5	265:19 266:16	224:19 236:20	personal 70:22	218:12,14
267:3 273:7,14	273:19 290:16	347:9 348:20	341:12	289:16 321:21
298:15 299:7,8	320:17 321:11	348:20 378:11	persuaded	444:15 461:19
299:10,13	326:10 341:13	378:19 396:12	129:5	placed 134:21
300:12 350:18	369:21 395:3,5	416:5 417:4	persuasive	135:16 500:9
401:5 439:19	396:5 400:12	420:17 425:24	131:5,10	places 233:21,24
440:6,17	402:7,9 424:2	432:9 448:9	267:24	289:14 298:17
443:16 459:5	438:8 445:23	perineum 130:2	pertains 90:20	plaintiff 292:14
470:5,13	470:24 479:14	130:13,16	246:20	plaintiffs 2:16
pelvic 487:14	490:12 498:23	131:19 330:13	pervasive	210:3 473:18

plaintiffs' 126:19 127:18 129:20 130:15 132:10 136:21 140:5 149:5 155:23 157:4 162:8 172:14 173:2 208:1,16	Plaza 2:4 please 11:17 12:4 16:5 57:23 74:10 108:8 126:9 138:23 146:12 146:24 152:9 159:23 163:11 163:12,23 166:12 167:17 170:18 171:16 188:8 190:24 195:19 233:1 246:16 253:23 291:15 306:17 343:18 442:2 443:17 457:1 458:14 462:13 463:16 466:23 472:16 516:3 518:3,8	264:18 266:19 279:17 280:13 347:13,24 349:18,19,22 354:2 379:9 380:17 391:15 392:20 400:6 400:10 410:10 427:23 428:2 438:10 439:8 445:17 446:12 515:20 pointed 392:16 463:7,17 pointing 279:15 463:21 points 118:10 120:11 polarized 399:14 policy 203:5 polite 163:23 169:5,17 polycystic 487:13 polyposis 456:6 pool 229:17 pooled 225:20 229:8 408:10 408:12 453:18 poor 285:8 poorly 308:12 308:14,16,17 popular 490:8 population 30:3 83:19,22,23 84:5,13 158:7 355:17 367:1,5 373:21 populations 82:15 233:21 311:7 381:17 portion 30:3 429:2 pose 169:13 posited 267:12 position 428:5	438:20 positions 465:13 positive 87:21 149:22 150:8 183:2,15 184:1 184:6,14 186:1 189:13 193:9 193:16,19 194:6,7,14 195:11,16,18 198:1,3,4 220:23 259:9 260:10 270:16 285:11 313:3 324:3 370:12 370:13,14,16 370:23 371:12 371:24 372:2 372:12 381:14 420:15 484:10 497:15 499:6 possibility 93:9 93:13,16 possible 13:22 95:8 129:1 224:20 228:4 252:24 253:1 272:3 333:10 363:2 400:11 421:5,7,12 422:11,14 469:13 possibly 52:12 201:11 277:9 278:2 324:14 419:24 420:2 502:8 postmenopausal 383:16 potential 151:20 289:18 352:5 425:15 487:19 potentially 338:3 487:15 488:2 510:24 powder 1:5 7:12 8:12 11:11	13:2,11 16:13 16:15,21 22:3 22:8,12,20 23:1 27:8 28:23 29:6,9 29:13,19 30:5 31:17 32:15 33:1,6 34:21 35:12,23 36:19 37:11,23 38:18 44:15 56:24 84:12 96:9,10 96:22,24 97:24 98:5 99:8 103:18 108:18 108:24 109:4 109:13,22 113:17 115:6 120:9 124:9 145:3,7,14 154:16 170:7 174:2,14,22 175:1,6,9,15 224:20 245:17 248:2 252:9 253:18 254:5 267:4 272:4 276:10,14 280:16 310:1 310:21 311:12 316:4 336:13 336:18,22 337:14 344:11 345:19 346:15 347:4,15 353:16,23 367:15 376:5 378:11 380:3 384:22 391:4 394:3 404:6,16 408:6 409:20 422:2,20 423:14 427:17 442:7 447:20 447:23 478:10 478:12,17,22 479:3,5,22
planning 125:14 144:1,12 145:10 plausibility 116:6 162:15 164:14,18 165:9,22 308:3 340:2 391:17 394:23 395:9 401:2 403:9 430:14 431:14 432:8 437:7 460:15 plausible 140:6 174:1,13 263:19 393:5 394:6 395:20 401:7,24 422:1 422:19 423:7 423:12 427:16 436:13 437:12 439:22 440:7 441:6,20 445:5 492:17 play 196:11 252:22 253:11 253:20 254:7 257:9 258:3 259:21 261:6,8 261:13,14,17 263:20 267:6 267:15,19 268:2,6,10 273:9 277:10 313:18 314:23 315:4 played 263:13 277:2 playing 390:4	pleural 9:11 465:2 466:10 468:1,6,17,18 469:11 Pleurodeses 9:10 pleurodesis 448:16 464:19 464:24 465:1 465:23,23 466:5,9 467:24 469:10,18 plus 114:11 307:24 pneumothorax 469:12 point 37:5 99:4 102:21 109:23 127:2 129:23 158:15 159:23 160:4,12 196:16,20 197:2,13,17 202:18 233:16 239:11 261:23 262:14 264:10			

480:23 481:21	250:2 261:1	255:9 277:4	122:20 140:19	391:4 394:4
482:6,11,15	355:2	320:22 357:21	151:4 159:6	408:6 480:14
483:12 487:15	pregnancy	479:11	248:11 270:21	481:6,22
491:4,14,16	487:9	prevalence	319:23 332:18	483:17 484:1,4
492:21 496:15	Prempro 243:18	248:1,7 260:13	427:7 430:4	484:5,13
497:21 499:5	244:11,20	prevent 37:4	495:17 513:4	497:15 498:15
503:16 504:14	preparation	455:19 456:8	problem 72:22	501:12 502:10
505:4 507:22	50:4 58:17	456:10 459:18	78:5 202:13	502:13 505:15
508:15 510:17	111:22 113:2	460:18	226:15,21,21	506:13
512:19 514:9	496:13	preventing	226:23 272:2	production 10:8
515:8,13	prepare 37:18	444:10	314:8 319:7,10	110:9 121:1,6
powders 84:7	56:2,21 59:8	previous 224:14	319:11 320:23	productions
power 318:21	prepared 56:9	previously	321:14 339:12	63:8
329:23 330:18	60:3	417:6 428:15	389:11 393:13	products 1:5,6
348:9 502:17	preparing 59:16	492:19	498:8	9:21 13:2
powered 325:20	59:20	primarily 307:5	problematic	16:13,16,22
powerful 266:22	Presbyterian	primary 79:19	80:7	22:3,8,13,21
455:18	301:6,17	84:4,8	problems 91:14	23:1 27:8
practice 12:16	prescribe 37:1	Princeton 3:13	198:17 309:15	28:24 29:9,13
12:17 25:23	243:17,20	printed 110:12	309:19 313:15	29:19 30:5
35:3 78:19	presence 132:7	printout 302:16	319:16	31:17 33:1,2,6
153:16 263:7	132:18 170:8	prior 13:20 39:4	proceeded 42:8	34:21 35:12,23
283:20 284:21	393:10,14,17	39:17 42:5	proceeding	36:19 38:19
288:18 304:2,9	393:19,22	46:9 59:4	102:19	44:15 84:2,12
306:5 307:2	394:19,24	64:17 66:2	proceedings	96:10,11,22,24
352:10 427:2	400:21 432:1	124:5,15,18	145:2	98:6 100:21,22
practices 1:6	435:13	125:2 139:20	process 15:3	108:18,23,24
28:13 204:4	present 4:8	169:1 181:2	115:13 118:13	109:4,14,22
practicing 12:13	170:12,21	230:8 233:7	118:17 144:23	113:17 115:7
303:23	184:23 224:17	234:14 256:19	209:7	128:19 145:3,8
pre-World 63:9	256:21 273:17	327:14 332:23	processing	145:14 154:16
69:9	448:18,21	358:24 404:8	400:2,7	170:8 174:2,14
preambles	450:11 451:10	404:17 443:20	produce 103:9	174:22 175:2,6
402:24	475:19,21	515:4	465:24	175:15 245:17
precancer	507:13	private 350:11	produced 51:11	248:2 253:18
451:12 452:1	presentation	376:6 445:2	51:18 55:21	254:5 345:19
precancerous	24:19,20	privileges 301:9	57:14 58:19	346:15 347:4
452:3	presentations	301:10,13,14	103:1 107:10	347:15 353:16
preceded 44:24	22:24 23:19	301:19	107:18 118:10	384:22 409:21
46:13	24:22	probability	154:7 186:14	422:2,20
precise 357:3	presented 54:21	272:20	318:10 463:24	423:14 427:17
precisely 379:8	164:4 179:4	probable 253:1	product 99:9	442:7 447:23
precursor	219:5 474:3	253:5,8	101:7 118:12	478:10,12,17
449:12 451:13	pretty 37:1	probably 13:18	144:15 251:3,4	478:22 479:3,5
predefined	38:20 39:4	25:10 36:15	266:3 267:5	480:23 481:11
197:24	41:17,24 57:7	38:4 39:13	296:10 310:1	482:12,16
predominate	57:8 254:15	59:22 106:20	316:4 367:15	483:12,23

484:18 485:2	154:24 354:3	152:3,12	243:4 304:9,12	61:9 63:20,24
491:4,14,16	442:18 446:5	176:21 317:24	329:23	64:2,24 66:20
492:21 495:22	prove 205:8	380:22 381:2,5	pursuant 1:13	67:16,22 70:8
496:4,15	393:23 396:24	381:6,22	pursue 210:4,4	71:22 75:23
497:10,17,21	433:19 434:7	publicity 272:3	put 27:11 81:17	76:8,15 77:22
498:2 499:6	437:9 438:9	275:12 276:8	102:1 187:13	80:10,17,21
500:10 503:16	477:7	278:14 279:21	221:15 222:16	81:18,22 82:4
504:3,15 505:4	proven 174:19	279:24	225:19,23	86:2 91:21
507:22 508:15	369:13 445:17	publish 144:5	239:8 285:8	98:4 101:12
510:17 512:19	456:15 513:3	281:9	290:10,12,15	105:2 124:14
514:9 515:9,14	proves 99:15	published 22:7	290:17,20	131:15 136:5,6
professional	174:17 280:9	22:12 44:17	291:1,17 303:7	139:10 159:16
1:16 242:18	provide 103:12	46:24 105:21	303:8 314:6,16	159:20 163:18
507:8 509:19	123:14 143:23	115:10 153:1	321:20,23	164:13 167:8,9
517:13	144:1,12	180:11 184:24	390:16 406:11	167:14,17,23
professor 287:2	146:14 171:6	200:5,7 240:3	436:24 438:19	168:2,4,18,21
prolonged	171:17 173:24	241:5 247:7	438:19 445:22	169:4,14,22
444:12	174:7,12 220:8	249:14 254:3	445:23 499:15	170:2 171:3
promote 173:13	231:1 235:5	287:3 298:15	502:9 503:14	175:10 182:14
prone 137:17	293:22 367:14	299:9,12,18,22	puts 77:20	189:24 190:13
226:9,10	432:18 433:10	300:4,9 363:23	262:18	190:17 191:2,5
307:14	433:14 504:3	382:13,17	putting 194:3	191:6 197:1,7
pronounce	provided 44:17	394:2 444:3	231:22 295:11	210:2,3 212:15
454:10	47:1,8 54:22	459:5 470:5,19	319:16 336:12	213:12,15,18
pronouncing	107:20 108:1	490:21 493:10	500:15,19	218:18,21,23
322:23	117:5,12 347:3	494:3	501:6,17	227:19,22
proof 254:14	433:20 478:8	publishing	pyramid 284:17	228:7,9,14
255:2,8,11	478:14,20,24	299:24		232:18,23
396:8,11,11	provides 177:16	PubMed 119:22	Q	237:16 246:16
425:14 434:9	393:5	120:3,23	Q-I-A-O 454:11	250:15 253:24
437:2 442:14	proving 410:12	151:10	qualifications	257:4 290:5
proper 66:4	433:14	pull 50:21 54:14	21:24 69:1	296:7 300:8
192:20 346:12	pseudoscience	54:15 55:7,8	quality 37:2	308:19 314:12
proposed	390:4 402:13	363:4 441:2	196:8 490:6	316:19 328:5
433:13,15	402:16,18	442:22 501:15	495:10	330:11 332:21
propounded	PTI 4:6,6	pulled 53:21	queried 367:1	354:6,16 357:3
520:9	public 1:17	pulling 58:21	question 15:21	365:2 367:6
prospective 8:6	144:20 154:19	466:3 500:16	16:7 21:11	371:22 376:4
100:9 101:1	272:7 350:10	Purdie 7:23	23:18 24:4,15	384:18 387:13
228:21 229:3	504:21 517:14	232:1 233:12	26:17 30:13	393:16 401:15
256:17,17	520:23	333:13,16	31:10,14,19	401:22 411:2
360:21 379:4	publication	334:2	32:1 34:20	412:24 413:1,8
380:2 381:21	124:20 181:2,6	purists 67:5	35:9 36:5	413:15 415:1,3
382:7 493:12	363:19,21	purpose 190:21	41:13,19 42:6	418:17 419:1
protecting	publications	298:1	42:17 44:3	422:7 423:21
504:21	22:16,20 28:17	purposes 20:15	45:17 46:14,15	431:3 442:19
protective	28:21 151:9	36:21 123:21	46:18 58:3	454:5 456:24

457:4,7,9	240:22	47:11,14 49:21	428:23 431:21	167:19 212:5
458:2,4,10	random 241:24	50:9,10,18,21	432:15,16	226:3 236:8
465:5 466:21	390:17	52:8 53:15,22	433:1 440:20	254:13 255:7
467:2,4,6	randomized	55:7,13,14	441:8 444:22	284:24,24
482:14 489:10	293:21 305:8	62:5,7 64:7,8	444:23 451:19	334:14 337:13
489:15 498:13	range 187:20	69:16 72:11	460:24 462:1	353:13 389:18
questioning	193:23 271:3	73:20 76:11,12	465:21 469:19	390:6,19
27:20 52:19	ranks 294:4	82:5 83:24	469:20 472:12	391:19 399:16
321:7 330:17	rapidly 293:9	84:9,19 89:9	487:16 490:16	410:15 449:11
331:14	rappel@seyfa...	90:13 118:15	504:10 509:6	456:2 465:15
questionnaire	3:19	119:12 120:24	510:13 513:24	502:20
344:13 366:22	rare 317:9	121:2 123:24	517:9 518:3	Realtime 1:17
367:3	rarely 316:17	124:6,20 125:4	520:5	517:14
questionnaires	rarer 260:16	137:19 138:8	reader 160:1	reason 34:7,11
265:22	rarity 325:17	140:16 143:18	reading 50:7	132:11 164:6
questions 10:14	Rasmussen	145:17,22,23	53:19 55:3,6	198:16 244:13
16:2 26:11	446:20 447:8	146:23 147:16	58:22 59:5	266:24 284:18
57:3 139:7	rat 129:12	170:24 177:12	73:2 75:11	311:2 320:19
159:14 162:11	rate 60:9 112:4	180:15 182:10	83:7 84:20	336:15 348:10
167:11 169:1	113:5 115:24	182:11 183:19	111:10 127:3	353:23 362:16
169:12 173:22	272:18 320:12	184:3 201:23	141:7,17 212:9	373:11 401:11
199:9 206:1	rates 248:11	201:24 203:7,9	215:7 265:16	448:6 457:14
216:15,21	ratio 192:14,21	203:15,20	274:9,19 297:3	459:15,16
258:14 298:6,7	241:23 243:23	204:8 211:21	314:17 350:22	465:8,11
298:10 307:17	244:8,11,17,22	212:13 215:7	350:24 407:9	466:17 467:3
328:3 342:6,7	245:21 249:6	215:12 217:7	446:12	467:13 483:18
353:13 354:13	325:20 329:18	220:3 224:22	reads 45:17	488:1 498:6
366:18 384:16	354:17 371:19	224:24 253:14	64:23 87:14	505:12 514:19
458:16 465:14	378:14 443:23	254:3 259:17	181:12 217:2	518:5 519:6,8
478:7 515:23	ratios 181:14	262:3 272:11	224:12 256:13	519:10,12,14
520:8	182:4 206:21	274:20 276:16	271:22 293:8	519:16,18,20
quicker 72:5	253:12 269:14	277:5 287:18	302:22 334:4	519:22,24
quickly 106:3	269:22 270:10	294:24 297:10	446:15 487:1	reasonable
159:6	271:1 311:22	297:11,11,17	503:24	90:12 158:9
Quit 215:16	408:13	297:19 302:19	ready 59:12	334:12 426:4
quite 61:6	rats 130:9	306:15 309:5	274:22	reasonably
quote 195:23	raw 178:17,19	313:24 334:14	real 226:19	158:24 280:10
329:7 439:2	reach 91:9 130:3	346:24 351:7,8	449:5	334:23
quoted 493:5	189:15 194:15	358:3,5,6,20	realize 48:11	reasoning
quoting 60:23	197:24 198:2,8	359:23 365:15	realized 122:22	164:10 258:8
329:8 382:8	260:17	366:9 374:6,10	314:7	reasons 99:13
	reached 74:22	378:22,23	really 20:10	216:9 269:23
R	75:14,24 85:15	380:15 397:6	59:19 61:4	423:2 460:8
R 2:8 519:1,1	195:17	398:15 402:20	99:24 100:2	reassurance
radiation	reactive 435:12	406:14 417:14	115:20 135:24	504:19
335:16 337:21	435:20	418:1 420:20	136:6 138:1	REATH 3:7
raise 205:24	read 31:5 41:12	421:4 427:22	144:16 166:24	recall 86:24

196:11 198:21	459:17 507:21	142:12 143:2,6	157:3 159:22	relating 108:4,9
198:21 199:1	recommendat...	146:3,14 152:4	163:24 171:9	142:8 162:14
226:10 251:22	455:21	172:5,10	172:5 187:19	relationship
252:5,11,16,21	recommendat...	313:17 347:18	237:22 241:3,5	46:12 70:24
253:20 254:6	495:18	348:4 424:19	243:5 267:4,6	100:5 316:3
254:22 256:8	recommended	referenced	287:7,19,22	393:24
256:13,20	456:9	49:23 50:11	308:21 334:5	relative 192:10
257:3,8 258:3	recommending	53:13 155:14	350:14,17	192:15 193:2
259:6,20 260:3	456:14	156:24 471:13	405:21 409:20	245:21 253:13
260:14 261:5	record 11:3,15	references	411:7 437:20	269:14 317:11
262:1 263:10	12:5 15:23	107:19 116:12	446:6 454:11	317:15 318:1
263:20 264:18	81:17 126:12	116:14,15	454:12 462:2	348:1,22
267:1 268:10	126:15 169:16	119:17 162:17	465:22 470:7	353:15 370:5
271:23 272:13	190:24 209:21	172:5	473:21 478:11	371:8 375:17
272:15,16,21	209:23 210:1,5	referencing	478:21 491:16	385:21,23
273:8 274:5,11	239:15,16,19	243:6 449:23	492:12 495:21	387:23 472:23
274:24 276:11	343:19,22	referral 140:23	496:3,5 497:20	474:11,20
277:1,7,10,12	348:12,15	referred 247:1,2	502:24 515:8	relatively 351:2
277:22 278:10	366:13 418:1	463:15 464:7	regarding 13:1	relevant 152:6
280:12 314:18	421:17,20	referring 39:9	22:2,7,12,24	152:15,19
346:21 347:5	453:6,10,13	65:24 68:16,24	38:18 108:17	154:12 224:19
407:12 428:1	473:8,11,13,23	88:12 140:21	171:7,18 281:6	reliable 177:3,7
460:2 502:8,8	485:24 486:3,6	164:1 243:2	287:4 293:13	177:11,16,22
recalls 497:8	517:6	244:4 260:5	419:5,14 469:9	178:11 188:16
receipt 518:17	redo 70:8	318:11 340:23	regardless	246:4 294:1
receive 105:16	reduce 447:12	409:1,10	307:15	308:8
105:22 106:1	449:8 453:17	462:17 509:10	region 271:5	reliably 77:16
114:16	reduced 455:5	reflect 111:14	registered 1:16	reliance 45:2,18
received 6:8	reduction	reflected 47:18	366:1,2 517:13	204:5 388:24
88:5,6 105:19	349:12 386:22	refresh 13:21	regression	441:1,15
106:6 110:16	386:23 443:21	38:11	296:10,11	reliant 392:11
114:15 121:11	448:2 454:18	refute 292:4	regularly 37:1	relied 45:20
rechurning	455:7	regard 22:20	490:16	46:23 52:8
225:14 227:10	refer 16:12	23:8,10,20	regulations	108:2 117:20
229:9 230:3,8	490:12	24:22 25:14,20	498:21 499:1	140:4 146:16
230:23 232:9	reference 47:18	25:24 38:12	502:23	relies 360:10
232:12 233:6	49:12,15,24	50:6 58:6 59:1	regulatory	rely 92:16
493:19	50:3 51:1,10	59:1,15 69:17	36:21 502:16	117:16 123:18
recognize 331:6	51:15 52:23	71:3 82:14	502:22	123:19 158:6
recognized	53:7 54:16	89:12,13,17	Reid 88:19	217:21 288:17
295:4	55:20 56:3,14	93:2 105:20	relate 18:4	307:5 372:4
recognizing	57:12,14 58:19	106:12 113:12	27:24 103:17	relying 333:17
331:7	69:21 105:5	124:7 125:5	107:11	remember 14:6
recollection	117:3,21	129:9 131:14	related 248:9	14:8 31:10
13:21 38:11	119:13 121:2	131:17 139:14	503:22	55:10 56:4
266:18	124:2 131:13	142:11,14	relates 1:8 89:19	58:11 117:11
recommend	139:17 142:1	145:2 148:23	305:19 306:1	121:20 122:2

130:8 141:22	16:18 49:13	405:23 406:12	478:23 517:7	restrict 64:6
171:1 189:23	50:9,12,19	407:5 411:16	requesting	89:24 137:6
218:22 254:12	51:5,6,16 53:1	433:5 453:2	331:14	156:21
255:6 262:22	53:20 57:13	454:24 457:18	requires 302:22	restricted 68:19
263:6 286:15	79:5 82:3	457:21 458:21	requiring	95:12
314:11 323:6,8	86:21 87:3	459:3,22	469:18	restricting
323:24 324:1	100:24 101:2	reported 132:8	requisite 346:3	66:22
374:5 406:16	103:24 104:2,6	132:17 181:14	research 7:16	result 154:23
434:16 435:3,8	104:11 105:6	182:4 248:19	22:2 101:8	203:3 204:4
435:11 441:14	108:6,10	311:23 354:19	145:6,6,13	347:3 360:20
454:8 478:1	110:14,20	381:16 384:21	153:7,12,20	resulted 276:9
remembering	111:21 115:1,6	391:22 397:8	203:5 288:8	476:14
254:17 272:17	115:10,15	417:1 435:2	292:23 293:11	resulting 174:15
remind 136:16	117:4 118:6,14	444:18	293:13,14	results 18:15
remove 126:10	119:3 120:12	reporter 1:16,16	302:23 461:2	101:10 116:3
render 160:2	121:7 124:5,19	1:17 11:16	researchers	179:18,19
165:9	125:3 126:19	15:16 185:8	205:12	203:22 204:2,3
rendering	127:5 134:8	232:19 517:13	resident 461:4	205:15 215:19
162:17 173:2	135:22 137:15	517:14,14,22	residents 23:7	217:16 267:7
RENÉE 3:17	137:20 139:21	reporting	resolved 14:1	274:6,11 275:1
repeat 30:12	140:10,15,17	177:23 267:6	respect 214:3,9	288:21 291:3
31:11 58:3	143:12 147:1	276:10 357:16	236:10 242:11	298:21,22
108:8 124:14	148:2 150:22	385:2 397:3,4	242:17 263:15	307:22 310:5
152:9 167:13	155:14 157:1,7	reports 8:6	352:22 489:2	322:18 357:9
170:18 171:16	159:24 160:17	49:21 50:7	494:8 495:5,15	358:13 360:13
188:8 212:17	161:3,10 162:4	52:2 53:12	respected	367:14 383:20
246:16 253:23	166:1 171:1,7	54:5 58:14,22	200:16,23	384:15 407:6
255:5 291:15	171:17 180:3	59:5 105:18	respectively	408:5,6,21
300:10 375:3	184:23 186:4	111:6 118:3	366:3	409:10 410:8
397:19 404:12	186:11 187:17	119:19 121:3	Respiratory 9:9	410:16 416:23
413:1,4 415:5	205:16 242:21	124:1 139:15	respond 139:8	442:24 444:2
442:2 467:7	243:5 245:11	143:19 504:1	168:1 328:4	469:13 475:22
481:14 495:24	250:6 251:24	represent 31:3	respondents	retained 37:22
Repeated	259:14 273:4,6	229:22 244:10	376:7	43:3 60:1
382:22	273:13,18	287:1 309:10	responding	Retire 6:17
repeatedly	274:4 276:19	407:23 424:16	376:7 458:9	200:20
48:13 49:2	281:2 286:6,8	503:18	response 79:7	retrograde
91:14	292:5 303:7	Representing	81:21 92:13	173:13 432:6
replacement	308:23 309:4	2:16 3:15,20	133:12 138:24	436:20 437:6,9
205:18 242:21	352:3 353:8	4:6	143:20 166:13	437:16,24
243:9	355:5 356:11	reproduction	297:4 306:17	438:6,16
replicated	356:17 357:8	517:20	320:12 479:6	return 518:15
161:18,21	357:22 359:13	reproductive	480:4 482:17	revealed 26:20
replication	374:12 375:5	25:3 444:11	responsive	reversed 357:15
217:15,17	384:9 390:23	request 10:8	81:21 457:6	358:9,17,18,23
reply 372:13	390:24 391:3	116:19	rest 314:16	359:19 360:14
report 6:10	391:10,20	requested	434:15	379:16 380:8

reverses 372:18	223:14 227:2	136:11 139:9	376:20 378:5	28:1 34:8
373:20 374:4	248:6 255:20	139:22 141:23	379:1 380:16	63:14 65:9
review 6:21 8:18	271:7 285:24	142:9 145:8	380:22 381:2	67:8 69:12,24
44:16 53:7,15	299:16 382:13	150:22 153:16	382:14 383:17	70:10,19 74:24
71:11 91:9,23	382:17,20	154:2,3 157:22	384:17,18,22	78:15 88:24
92:19,23 94:11	383:6 388:19	161:18,22	387:2,8 390:22	89:4 90:14
94:24 95:18	403:12 437:19	168:24 176:18	395:11 400:2	94:12,14 95:15
97:17,24	470:18 481:13	176:23 186:14	402:9 404:24	98:17 124:10
102:19,22	483:16 484:7	186:19,22	405:3 412:3,20	149:8 174:23
103:2,8 105:21	508:23 511:12	187:22 192:11	415:9,10 416:5	175:11 183:3,5
111:2,6,20	reviewer 176:21	193:6,6,7,9,17	416:6,9 417:11	183:16,18,18
126:21 127:14	178:6,14 179:2	198:7 201:15	418:12 420:10	187:20,22
128:6 129:9	180:21 181:3	202:5,6 203:19	423:16 424:6	188:18,21
131:2,6,16	reviewing 58:13	206:15,18,19	425:9 426:14	189:18 192:15
139:12,19	115:17,21	207:11,17,19	426:16,17,21	193:2,22 196:9
142:22 143:16	119:18 161:19	207:20 208:20	428:7 430:16	196:17 197:3
149:3 150:5	162:9 178:23	209:11 213:13	431:22 436:9	197:18 198:20
154:5,20	284:5	215:2 229:24	443:6,14,23	203:24 205:3
162:13,16	reviews 304:5	239:15 241:20	444:6 445:1,9	206:10 210:18
165:8,21 166:8	304:21 305:1	245:17 247:9	445:15 446:13	210:23 226:5
168:18 170:6	307:11 491:12	249:1,4 255:20	449:23 452:16	226:14,22
180:20 181:1,5	revisit 66:24	265:2 271:8	466:10,14	229:15 243:5,8
196:6 247:22	RICHARD 3:12	275:5,6 276:3	467:10 468:22	243:11 244:21
289:11 299:7	richard.heasli...	279:12 281:7	473:4,6,10	245:5,15,19,21
336:20 440:14	3:14	287:12 294:14	474:5,12	246:4,13,19
440:22 485:13	rid 219:19,23	295:9 298:11	476:11,22	247:10,10,20
490:18 492:1	220:1	298:14 299:18	477:18 478:3	249:6 252:9,15
514:23	ridiculous 396:2	300:6 301:5	481:8 483:10	252:19,22
reviewed 6:8	right 15:1,6 16:9	303:19 305:2,3	486:19 487:5	253:18 254:5,8
15:3 46:7	21:2,20 22:9	305:5,14,21	488:4 490:23	260:19,23
51:14,24 52:1	29:1 30:5 33:2	309:4,20 310:2	494:22 497:3	261:9 269:3,14
52:8 53:3,10	33:6,23 34:2	313:19 315:22	502:19 505:5	272:22 273:10
54:10 56:17,19	34:10,12,13,15	316:20,21	507:3,6 508:12	309:24 310:1
56:22 57:7	34:16 37:13	319:6 322:5,11	515:19	310:10,15,20
58:17 91:12,13	42:24 43:2	322:15 325:5	right-hand	311:1,9,11,19
92:8,22,22	45:14 47:5	329:20 331:10	87:13 182:20	312:1,12 315:8
105:4 106:13	52:10 64:20	332:15 333:6	215:15 217:10	316:4 317:11
110:17,19	68:7 69:4,18	334:18,22	271:18 275:16	317:15 318:1
115:17 117:16	73:22 74:15	343:4,5,6,11	351:1 377:4,5	319:23 324:10
117:22 131:12	80:22 82:12,18	344:13 346:10	377:21 378:5	324:15,18
133:1,21	83:10,13 86:17	347:2,13 348:2	risk 6:23 7:7,10	328:22 330:4
136:23 142:12	88:1,3,9 96:17	348:6 350:8	7:21 8:9,12,15	338:5 339:11
143:8,11,15	97:1 98:7	351:22 355:8	9:13 13:2	342:4 343:7
144:3,17	102:5 109:23	360:4 363:12	17:10,14 23:4	348:1,5,22
146:16 148:22	112:7 124:10	365:18 368:6	23:10,11,20,23	349:3,9,10,12
155:24 167:22	127:6 134:18	368:12 374:10	24:7,9,22	349:13,14,16
219:4,9,17	135:1,9,13	376:14,15,18	25:14,24 26:9	353:15 355:6

356:9,19	routine 27:20	sample 317:22	330:22,24	336:1,1 338:24
357:24 360:23	routinely 279:9	328:20 375:14	337:2 339:23	351:16 359:18
363:2 370:5	Royston 4:6	samples 478:11	340:4 341:21	365:21 373:21
371:4,8 373:6	rubric 36:20,24	497:15	361:1 362:12	379:3 399:4,5
373:23 376:23	rule 320:16	San 2:9	363:1 375:12	416:15,22
378:13,17	ruled 94:17	sand 87:6,8	387:19 392:21	421:12 425:10
380:3 382:8,9	272:18	Sander 199:18	395:3,12,19	437:10 444:7
386:23,24	rules 236:11	201:5 287:9	399:3,8,9	457:21 469:7
405:9,11,15	285:2	sanitary 354:1	413:5 418:3,8	471:5 473:3
419:6,18	S	saved 106:17	422:14,15	476:13 488:20
443:22 444:20	S 5:10 6:2 7:2	saw 72:15	425:21 426:2	498:22 502:12
446:17 447:12	8:2 9:2	135:21 144:15	437:5 438:24	503:21 508:10
448:2 449:9	S-T-R-A-U-S	149:4 238:10	451:24 455:1	510:22 511:5
452:14,20	303:4	260:22 314:5	458:20 460:11	511:12 513:23
454:18 455:14	Saed 124:7	364:17	460:13,22	scenario 330:16
455:24 456:16	139:20 140:24	saying 50:17,18	474:16 476:2,4	493:24
457:12 459:8	162:16 165:24	53:16 56:5	477:13 489:21	scenarios 275:2
469:13 470:7	432:17 433:2	62:11 66:14,19	493:18 496:15	Schildkraut
472:23 474:11	434:13 492:16	76:17 79:24	503:15 505:2	7:15 254:14
474:20 479:15	Saed's 124:20	86:4,9,10	508:1,7 509:2	255:8 261:15
479:19 484:14	125:4 140:12	91:15 92:6	510:7 511:2,8	264:22 268:3
485:9 487:6,20	493:4 495:11	98:19,22 100:4	512:11,12,15	273:22 275:3,8
493:15 498:17	Saenz 54:20	100:10 106:23	513:16,22	275:14 278:19
507:12 514:2,5	146:9 147:2,19	127:12,13	says 36:10 68:12	280:14 314:19
risk/benefit	461:1	129:24 131:1	72:13 74:6,16	Schildkraut's
33:22 34:4,6	Saenz's 55:3,6	134:1 144:14	74:21 75:20,21	264:20 268:5
risks 75:15 76:2	111:11 142:23	165:19 177:21	75:23 76:18,23	268:12
85:16 192:11	143:8,14	178:16 183:6	77:1,20 82:6,8	school 301:11
243:23 253:13	Saez 163:19	184:5 185:17	82:11 83:16	350:10,12
robbed 395:21	safe 226:17	189:17 194:1,5	84:1,2 85:14	372:7
ROBINSON 2:3	239:8 479:5	195:7 197:15	88:4 90:13	school's 301:12
robotic 14:19	480:3,24	205:1,2 230:5	127:7 133:20	schooling 445:2
robust 231:2	481:17 482:3	230:12 231:12	147:1,9,15,17	science 57:2,5
Roggli 468:24	482:14 483:7	232:13,14	158:10 182:1	57:17 58:5,24
role 39:9 98:14	484:1 499:21	233:8 257:20	183:22 184:6	59:1 153:12
157:20 181:3	500:12 505:2	257:24 259:20	184:13 196:5	205:11 217:21
196:11 277:3	508:15 510:3	276:21,22,23	202:13 203:17	398:9 400:16
room 15:12	514:8,15,20	277:1,3,5,11	236:17 237:6	461:2
ROS 125:5	safer 506:3	277:13,16	247:19 253:11	Sciences 446:19
435:4	safety 196:14	278:2,10,11	259:2,4 267:18	scientific 104:21
Rothman 7:17	205:19 427:4	294:14,16,22	271:20 275:21	111:3,4 115:11
199:21 286:21	428:11 504:22	296:1,8 299:6	277:17,20	156:2,13
287:8 288:7	506:20 510:17	299:15,17	290:12 292:4	157:10,14,16
292:16,24	sake 352:13,23	311:2 312:24	319:12 321:1	157:20 217:22
294:2 298:14	481:14	313:7,8,10	321:19 322:12	293:8 341:18
roughly 113:20	SALES 1:6	314:14 315:1	322:14 323:15	428:10,20
routes 84:8		327:11 329:9	329:5,5 331:1	430:8 504:8

scientist 178:19	42:17 53:8	415:24 416:9	136:23	sets 350:3
scientists 67:6	54:12 74:6,18	416:20 425:6	seminar 201:18	setting 15:12
154:19	75:7,11 85:9	428:17 429:1	Senate 154:11	64:3 68:19
screen 73:19	94:19 99:11	436:5 439:1	send 208:20,21	71:2 77:13,15
256:1,2	116:4,5 121:14	442:23 445:21	sends 198:22	492:3
screening 6:19	127:11 129:11	446:14 449:21	499:18	settings 63:4
142:13 220:11	132:15 134:22	450:5 451:3	sensational	64:5,9 68:20
scrub 450:10	137:14 149:15	460:20 461:7	490:8	70:21 71:3
se 264:7,7	150:2 151:2,3	461:10 469:1	sense 185:19	80:1 86:7
Seaport 3:4	153:17,17	471:24 472:14	226:3 270:24	88:23 89:5
search 120:2,5	161:11 180:18	476:19 480:17	371:15 395:23	90:3,5 101:23
120:21 282:13	181:20 182:17	488:18 491:20	461:19 500:5,6	seven 270:22
282:18,24	185:22 200:19	497:2,5,7,11	sent 106:24	SEYFARTH
283:3 286:12	201:2,5,8,12	497:13 498:20	sentence 181:10	3:17
288:4 362:15	201:14 204:6	503:9,10,15	275:17 310:17	SGO 507:3,14
searched 282:10	210:15 214:8	508:20 511:1,6	378:8 476:13	507:19 508:7,9
searches 119:22	214:22 215:24	511:22	separate 204:15	509:19 510:4,6
119:22,23	216:10 219:22	seeing 127:9	222:14 301:7	510:14,20
120:19	226:13 229:16	323:6 449:24	381:12	511:1,20 512:2
seats 73:19	232:1,2,3	450:20 451:2	separated	512:12,18,24
second 141:12	236:6 250:18	seeking 154:11	186:13 264:22	513:18,23
141:16 164:8	256:9,11	361:24	488:1	shaded 186:17
192:24 213:15	258:23 259:1	seen 19:8 46:8	separately	186:22,24
213:18 232:24	259:21 261:13	128:24 132:10	222:14 322:1	187:2,3 189:20
269:19 274:18	264:8 269:11	180:17 197:16	serious 203:24	shakes 389:17
287:9 334:9	269:24 271:19	247:15 248:23	seriously 321:3	share 322:17,20
348:8 350:9	275:8,19 280:1	260:15 263:17	serous 8:21	322:21 504:7
354:20 367:19	287:8 288:15	292:24 318:8	21:16,19	Sharko 3:8 31:1
370:10 374:24	290:7 293:4,6	359:15 394:1	249:20 256:22	31:6 57:21
384:3 409:17	294:7 303:6	411:22 422:8	259:10 260:12	58:1 66:6
417:14 425:2	308:22 309:13	423:8,10,24	260:24 311:1	71:16,19 73:12
425:11,12	313:16 318:16	424:3,5,7	353:16 354:17	73:18,23 76:19
443:18 473:5	318:23 319:14	440:17,19,23	354:22 355:10	80:16 81:5
475:6	323:3,7 325:6	448:7,22,23	356:19 357:9	163:20 168:24
Second-to-last	325:8 333:17	449:1,12,14	357:24 370:7	169:3,18,19
476:12	333:19 334:15	450:15,17,19	372:11 378:13	170:3 190:9
section 84:24	335:14 336:21	451:17 452:2	378:18,20	191:2 207:23
134:9 159:24	350:6 355:15	454:9,15 463:1	409:5,6,21	208:10,15,18
160:11,13,15	357:11 358:21	463:4 470:17	410:19 448:19	209:1,11,14,17
160:17,23	362:4,13	470:23 486:17	449:13 451:14	209:24 213:16
161:20 162:4	365:21 367:24	492:1	461:13 476:17	213:19,24
163:4 172:11	373:10 378:4	segment 215:12	served 176:20	214:2,10 357:4
172:21 189:8	381:9,24 384:2	selection 361:5,9	services 1:20	377:22 378:2
202:12 374:7	389:2 397:23	selective 126:21	11:5 111:17	414:24 458:12
429:8 431:14	398:8 403:8	127:14 131:1,3	serving 515:13	468:10,13
sections 450:11	407:15 408:11	131:4	set 108:5 288:20	473:13
see 31:13,22	408:15 415:17	selectively	401:5	SHAW 3:17

she'll 169:5	320:12,13	signatures	518:10	292:22 293:14
sheet 518:7,9,12	339:9 355:6	448:24	silence 169:21	338:2 345:1,4
518:15 520:12	356:18 392:9	signed 115:2	similar 66:21	471:19
short 126:13	433:16 443:21	214:19 338:14	226:14 230:21	size 182:24
343:20 351:2	453:16	340:8 352:18	238:3 256:21	183:14 185:22
352:16 421:18	Shower 16:15	significance	257:7 294:22	205:5 290:7,15
486:4	16:16,21,22	6:17 150:15	410:16,24	290:15 313:23
shortcomings	97:20,20	188:3,14,17,20	411:6 420:1	314:2,8,9
398:18	showing 21:8	188:22 189:3	501:20 502:3	317:16 318:17
shortened 272:5	65:17 66:1	191:12,16,24	Similarly 500:8	318:22,24
Shorthand 1:16	88:7 89:3	192:2 194:16	simple 136:6	375:15,18
517:13	127:23 128:8	195:17 198:8	166:16 190:16	sizes 205:2
shortly 270:18	134:2 164:10	199:13 200:21	259:5 299:19	317:22 328:20
show 55:12,13	187:7 188:18	204:6,19	simplex 120:14	slides 450:1,13
77:14,23 82:13	204:3 207:9,10	210:20,22	simply 82:4	450:16
89:5 90:6	210:21 238:15	214:17 215:20	single 55:14	slowly 293:11
128:10 129:14	273:18 339:16	217:20 218:1,9	110:11 128:12	small 133:1,21
130:12 131:9	410:11 424:9	218:13,16	243:1 250:20	134:1,4,5
132:12 149:2	425:24 426:7	219:24 220:2	250:24 309:11	182:24 183:13
150:13 180:1	427:9 451:20	236:3,6 287:11	312:13 313:16	204:24 205:1,5
183:2,3,4,15	455:4 461:10	298:20 311:5	329:12 426:7	226:14 314:4
183:17 189:2	479:13 484:11	477:9	439:1	314:10 317:16
191:11,15,21	shown 64:5 90:3	significant	sir 147:10	317:24 330:4
191:23 192:2	100:6 130:17	150:1 183:3,8	sister 311:7	375:18 420:14
199:12 204:4	158:2,4 222:15	183:9,16 187:6	sit 119:2 229:17	431:7,12 472:3
205:12 221:3	229:14 438:14	189:11,18	472:6	smaller 260:17
222:11 233:14	439:3 456:2	195:2 203:3	site 281:19,19	386:9
243:8 245:18	465:1 470:11	204:16,17,23	507:14	Smith 156:18
260:18 261:12	shows 22:6	210:11 216:4,5	situation 64:1	157:5 292:4
262:16 269:17	98:17 129:1	220:23 238:16	67:11 78:2	smoke 342:16
280:2,3 287:5	133:6 149:8	241:22 243:8	90:15 128:13	342:24 343:1
310:5 333:16	210:20 261:17	254:16 255:9	262:11 331:21	smoking 306:20
339:18 346:19	344:23 363:1	272:22 280:15	356:5 392:13	342:5,15
347:8 362:3	384:20 393:3	296:12,17,18	394:17 396:2	487:11
365:11 408:5	Shukla 139:13	298:22 317:15	482:21 483:9	snapshot 450:24
421:4,11	162:16 163:19	323:23 370:15	493:7 495:1	snide 214:7,11
445:23 447:11	165:23	370:17 371:1	502:6,11	Society 176:18
455:1,7,13	side 81:7,9	371:10,20	situations 61:19	507:5
457:12 459:8	110:13 215:15	374:15 375:9	63:11 67:10	sold 496:4
462:11,14	378:6 506:20	386:21 420:15	69:15 77:17	somebody 78:21
463:8 470:13	sides 110:12	433:21 443:21	90:10 100:7,12	149:16 250:21
472:8,16 474:3	198:20 455:10	443:23 472:23	326:22 333:4	267:17 336:12
479:17,19	sign 517:9 518:8	474:12 475:21	335:15,18	338:17 339:4
showed 70:18	signatories	476:15	337:3 442:16	340:5 361:24
130:3 149:22	201:9 203:12	signing 124:5,18	456:7	369:14 373:13
150:4 151:24	signature	125:2 139:20	six 7:16 75:16	403:5 511:10
203:23 282:5	451:15	165:24 352:20	76:2 85:17	someone's 132:7

someplace 430:1	141:10 177:3	speculate 413:6	338:15 339:1	335:12,22
something's	259:7 260:4	speculating	340:7,13,18,19	356:24 371:14
300:4	290:24 291:9	412:18 414:17	341:24 342:14	374:21 375:3
somewhat 248:8	291:12,13,21	speculation	342:21 352:17	379:24 380:18
284:20	291:23 292:2	413:5	370:3 383:23	396:3 404:13
sorry 14:7,9	sources 84:4	speed 463:11	400:20 405:3	425:22 430:21
30:22 38:7	278:12	spend 164:17	502:21	435:11 437:14
40:11 72:19	South 4:3	403:10	starting 428:17	502:21 511:4
75:1 82:16	space 518:6	spent 61:6 137:9	starts 266:13	511:14,17
92:10 124:13	speak 67:12,12	361:4 409:13	340:11 341:22	513:19
124:24 125:16	70:23 81:12	sperm 173:13	403:5	statements
136:2 142:20	209:3	spirit 233:22	state 12:4 95:7	88:17 138:10
151:14 175:9	speaker 201:19	split 266:14	126:18 140:10	158:6 162:8
180:9 181:15	speaking 21:14	273:18 279:6	145:2 161:3	181:8 182:17
192:23,24,24	65:20 211:18	310:24 392:18	172:15 182:7	217:15 297:7
218:20 220:1	408:22 457:14	476:5	190:23 267:3	325:22 326:11
224:13 237:14	457:20 463:16	split-off 475:1	334:10 350:17	328:7 394:11
237:17 255:22	490:4,6	splitting 324:1	351:2 357:8,13	402:23 423:22
261:7 269:4,5	special 268:4	474:24	357:23 358:9	495:20 496:3
269:14 274:8	specialist 42:10	spoke 410:2	376:21 403:1	States 1:1 29:18
274:14 275:23	91:5	spoken 147:23	436:10 492:9	30:4 32:13
280:22 283:6,7	species 435:12	spontaneous	518:5	145:1 154:11
293:19 308:18	435:20	469:12	stated 46:15	240:13,16
310:18 322:23	specific 21:13	Sprague 130:9	191:7 275:11	248:1 249:1
325:9 327:20	31:22 32:9,20	spurious 116:3	288:3 307:10	stating 100:3
328:1 329:5	37:6 53:24	196:10 205:9	357:21 358:2	201:17 261:5
334:6,13 344:7	58:7,11 61:18	274:6,11 275:1	413:13 445:5	394:5
345:2 347:21	63:10 64:9	320:2 360:20	457:18	statistical 6:17
348:8 350:19	67:4,10 69:14	SR 304:20	statement 23:22	18:5,7,15
350:21 354:20	70:20 71:3	stage 466:14	49:16,20 80:12	150:15 188:3
364:9,10 366:8	94:5 160:23	467:9,19	93:21,22 99:23	188:14,17,19
367:20 370:10	168:13 283:23	Stand 343:18	133:20 140:14	188:22 189:3
374:18 377:7	413:15 428:22	348:11 516:3	140:22 141:11	191:11,16,24
377:13 383:18	432:10 440:10	standard 495:10	149:6 161:6	192:2 194:16
403:16 415:19	440:21	stands 507:5	182:13 184:4	195:17 198:8
415:21 425:1,7	specifically	start 21:7 25:18	185:17 195:20	199:12 200:21
426:18 429:18	59:11 93:15	87:13 110:13	197:17 199:7	202:3 204:5
430:1,13 443:1	111:8 152:2	120:21 183:11	212:18 225:10	210:20,21
445:7 446:24	160:12 164:2	244:6 325:11	247:13,14	214:17 215:18
462:8 465:12	171:9,20 191:8	326:1,4 336:24	249:10 255:5	215:19,20
470:1 489:12	247:23 278:21	337:1 338:12	260:3 266:22	217:19,23
sort 34:14 66:13	308:24 316:2,8	369:18,23	267:21 277:11	218:1 219:24
98:10 352:6	490:5	487:3	285:18 286:4	220:2 269:7,8
374:13 449:4	Specificity	started 84:20	291:7,22	287:11 298:19
477:15	429:22	113:3 115:16	292:12,13	298:21 477:9
sound 358:23	specifics 252:5	119:2 166:22	295:2 299:6	statistically
source 140:13	specify 243:2	194:24 299:5	318:4 330:14	150:1 187:6

201:21 203:3	510:5 512:15	425:22 453:24	186:17 187:1,2	306:22 307:4
203:22 204:16	512:19 513:1	456:8	187:19 188:3	307:12,15
210:10,11	stopped 300:14	stronger 205:8	188:14,16	308:8,9,22
216:4 220:22	345:18	229:14 484:11	189:1,2,22	309:16,23
241:22 272:22	stopping 37:6	strongest 249:21	191:10,15,20	310:4,5,6,14
280:15 296:12	store 498:9	259:10 260:11	191:23 192:10	310:19 311:3
296:17 309:24	stores 498:9	strongly 87:21	192:16 193:5	311:15,16,17
370:15,17	story 185:7	struck 423:20	198:18 199:12	312:11,13,19
371:9,20	239:2 484:8	struggles 339:23	203:2 205:22	313:2,4,5
374:14 375:9	strange 410:6	stuck 300:11	207:8 210:10	314:5,15,17,22
386:21 420:15	strangely	students 23:6,6	211:9 217:17	315:4,7,11,24
433:20 443:22	353:22	studied 77:12	220:21 221:15	316:2 318:18
472:22 474:12	Straus 7:20	100:13 253:17	222:5,6,11,16	319:1,21
475:21 476:14	303:4	322:11 481:11	222:18 225:23	320:23 322:9
statistics 193:15	Street 2:14 3:13	studies 18:6	226:4,20	324:4,9 325:2
194:3 219:19	3:18	31:20 44:17	227:14 228:2	325:16,19
219:23 283:19	strength 164:7	46:24 47:17,19	229:3,12,14	329:2,4,16
284:10,13	246:14,18	48:2,24 50:10	230:1,6,18,22	330:1 339:16
286:14	268:19 307:23	58:7,11,16	231:10,11,13	340:16 355:6
stay 28:24	408:23 409:11	67:4 76:6	231:16,21,24	355:16 359:22
steady 328:14	429:10	78:10,14 87:22	233:11,13	360:2 361:6
328:15	strengthened	88:6,21 89:3,4	234:3,11,12,14	362:14 380:6
stenographic	361:21	90:6 91:16,18	234:15 235:2,5	380:10,24
11:15	strengthening	93:14 94:8,19	235:16,20	381:6,12,16,19
step 479:7	361:17	95:13 98:16	236:14 237:3,4	390:7 392:23
Stephanie 487:2	strengths	100:9,20,24	238:3,12,12,15	395:6 405:21
stepping 66:22	115:22 282:2	105:5 106:6	240:2,4,7,8	406:4 410:4,4
Steven 180:13	284:22	111:3 115:18	241:11 243:7	410:9,14,24
426:19,24	stress 480:18	115:24 116:2	245:18 247:7	411:5 424:9
428:9	stretch 369:10	121:4 126:23	248:6 249:20	425:23 438:9
STIC 448:19,23	369:17	127:14,17,23	252:8,15,17,21	438:23 440:6
451:11	strict 285:1	128:8 129:2,8	254:3 255:13	440:17,19
stick 245:12	strike 43:18	129:13,20	256:15 257:6	446:3 452:13
330:13	55:4 67:19	130:6 131:8,14	259:2,4 261:9	453:20,21
stimulate	76:17 80:15	132:3,15,23	265:16,21	455:3,6 457:12
293:12	144:9 157:2	135:15 136:7	266:14 268:11	459:5 461:10
Stipulations	158:22 163:16	136:12,23	269:11 270:2	470:13,18
10:11	191:21 206:5	137:9,14,22	270:16 271:3	474:17 479:13
stop 9:20 163:12	212:20 213:17	148:22 149:11	272:1,23 274:7	479:16,19
202:14 205:22	241:18 287:20	149:12,15,21	274:12 275:1	484:9,11 490:7
208:8 209:2	336:15 356:14	150:6,14	282:9,20,21	493:13 506:11
283:17 458:14	418:22 423:9	153:16,18,19	283:4 290:6,8	506:12 509:9
465:19 497:9	430:24 446:8	164:1,3 165:21	290:17,20	study 6:15 7:14
498:22 499:15	447:21 450:18	168:11,12	291:1,17,24	8:6 20:13
499:16,19	456:19 459:20	170:14,22	293:23,24	31:22 53:13,15
501:7 502:1,10	strong 89:3	182:6,23	294:4,5,12,12	53:19 77:13
502:13 509:21	116:1 285:6	183:12,23	304:1 305:10	86:4 90:13

91:2 118:15	311:7,8 312:5	381:4,5,21,21	252:4 257:2	suggesting
126:21 128:12	313:11,21	382:4,7,13,21	518:10	133:2,22
128:24 129:24	315:12,13	383:13,15,15	subjected 269:8	187:21 257:6,8
130:1,16,19	316:12,16,18	383:24 384:9	410:14	299:24 399:7
131:7 132:5	317:8,10,16,24	384:21 385:18	subjective	405:18 422:16
134:16,16,19	319:6 320:1,12	387:2 388:3,9	263:24	423:24 484:9
134:20 135:1,2	321:5,12 322:9	388:12,18,19	subjects 289:14	502:5 508:3
135:8,12,23	323:2,5 329:12	388:23 394:2	submitted	suggestion
136:11 147:23	329:19,20,20	395:13 397:2	176:21 178:15	169:16 398:9
151:17 161:20	329:24 330:3	397:21 401:4,5	submitting	445:16 476:18
167:22 168:19	330:24 333:13	401:23 403:13	178:18	476:22,24
170:13,21	333:16 334:2	403:14,17	Subscribed	477:3,13
172:10 177:3	337:13 338:1	404:1 405:10	520:19	suggests 326:5
179:22,24	338:13 340:12	405:13,18	subsequent	405:10,13
180:13 184:9	341:3 344:2,9	406:12 408:10	224:16 225:12	Suite 2:9 3:13
184:18 189:13	344:10 345:19	408:11,12,12	227:23 228:24	4:4
189:17 190:19	346:3 350:1,6	410:7,14	229:2 233:5	summaries
193:18,20	351:10,14,22	411:10,13,16	subset 310:23	305:7
194:6,14 195:9	351:24 352:6	411:18,19,21	substance 19:10	supervision
195:11,16,18	353:7,22	412:10,20	97:9,11 485:9	517:22
196:8,9 197:22	354:19 355:22	413:17 414:5	485:11 520:11	supplemental
197:23,23	356:18 357:16	414:10 423:8	subsumed	6:7 49:15
198:1,3,6,12	358:1,9,10,16	423:10 424:5,7	450:23	51:10,17 53:1
201:1,3,6	358:19,21,23	426:7 427:9,14	Subtype 8:10	54:4 55:20
207:10 210:17	358:24 359:16	428:18 431:16	sudden 262:20	56:3,14 57:13
212:16,21	359:19,20	433:20 434:6	263:5,8 280:6	110:16,19
215:1 219:3	360:3,7,10,10	435:24 437:2,8	sued 13:13,24	116:14 117:5
220:7,18 223:2	360:12,22	439:1,7,18,19	sufficiency	121:1,7,10
226:8 236:18	361:14,18	440:6,13,21	246:3	124:2 146:20
238:6 240:4	362:21 363:22	443:2 445:4,13	sufficient 93:18	155:15 459:22
241:7,12,16,21	364:4 365:6,7	445:13,21	247:11 313:23	463:22
248:18 254:12	365:22,23	446:23 448:11	325:14 329:17	support 10:2
255:7 256:6,17	366:13,18	453:1 454:11	330:2 336:21	88:6 89:8
256:18 257:5	367:10 368:14	454:16,16	479:21	140:5 150:13
261:3,12,13,16	368:21,22	465:22 467:23	sufficiently	194:19 199:11
262:2 264:1,20	369:3,20 370:2	472:19 476:10	325:19	231:2 268:18
267:3 268:5,7	371:18,21	488:14 489:20	suggest 31:20	276:11 277:21
268:12 273:6,7	372:4,12,18	study's 344:16	149:24 276:8	292:13 307:6
273:14,14	373:6,10 374:1	studying 254:4	300:3 397:12	309:23 310:9
277:12 282:2	374:9,9 375:6	394:3 396:4	397:22 398:6	310:14,20
283:21 285:6,8	375:15,18,19	stuff 107:8	398:16 399:2	311:9,11,24
285:11 286:1	375:23 376:3	390:10 482:24	400:13 420:14	312:12 412:9
287:6 289:5	376:22 377:6	498:18 506:8	422:12 450:20	433:22 437:11
293:21 300:16	377:20 378:9	subgroup	479:22	441:21 446:16
301:24 302:5	379:1,4,7,10	249:18 387:14	suggested	448:1 455:18
308:1,10,12,15	379:11,17	subject 107:15	256:24 352:8	460:14 502:14
308:16 310:22	380:2,21,22	116:2 211:10	445:8,8	supported 61:4

89:2 91:16	471:22 472:24	T-A-H-E-R	342:2 343:16	249:5 250:5
supporting	474:14 475:7	223:17	355:18 357:11	254:17 256:15
124:8 438:23	483:10 485:6	table 6:15 148:3	376:17 389:17	256:22 257:1
supports 66:14	490:4 493:8	148:6,7,8,18	389:18 421:13	265:10,23
194:13 360:22	496:1 498:5	148:21 150:12	449:18 450:15	266:10,18
432:7 437:7	501:2 506:6	186:4 187:9,14	453:8 455:23	278:14 307:20
supposed 54:13	507:17 508:9	190:18 192:9	456:1 485:20	311:24 330:12
54:13 89:9	511:19 515:22	204:11 219:6	taken 1:13 15:6	331:16,18
504:21,23	surely 360:12	240:3 269:13	45:13 196:21	339:5,24 340:7
supposition	surface 123:5,11	344:23 347:5,9	249:10 326:23	340:18,19
97:15 98:23	398:19 399:18	347:9 350:3,6	375:22 444:15	341:7,14,23
99:6	399:22	363:3 367:22	takes 26:22	344:24 347:10
sure 24:17 29:4	surgeries 400:9	384:20 415:20	226:22 369:16	347:14,14
29:22 30:14	surgery 14:19	471:18,18,21	talc 6:13,23 7:6	348:20,21
31:13,24 33:17	450:8	471:24 472:12	7:10 8:7,14,17	351:19 352:18
33:21 35:9	surgical 400:8	473:3 474:3	9:10,13,22	352:19 357:17
38:24 40:10	surprise 226:3	475:15,19	16:19 23:8,14	366:19,20
57:24 59:17	surprised	tables 324:7	23:23 24:21	367:2,6 368:1
66:8 71:15	226:12 236:5	Taher 6:24	30:9,16 32:4	368:21 369:18
72:24 79:16	surprising 183:1	145:17 146:2	34:21 43:3,14	370:3,6 374:16
85:8 99:13	183:14 225:13	147:23 171:10	44:3,23 46:12	383:24 384:7
108:9 124:17	232:5 250:1	171:21 223:14	56:23 75:17	389:24 390:20
125:12,18	260:20 311:21	223:17,18	82:23 83:23	391:5,12 393:4
127:2 132:1,9	surprisingly	224:3 231:20	84:4,22,24	394:4 396:1,6
136:4 144:4	311:13	234:6,7 259:11	85:20,22 86:16	396:12,20
147:16 173:19	surrounding	261:21 321:10	89:18 95:1	398:20 400:22
188:10 193:3	468:20	323:21,23	96:2,6 97:18	404:4 405:3
195:21 216:23	Susan 3:8 80:23	324:5,6 325:7	97:19 98:20,24	416:5 417:1,2
222:1 235:3	125:21 208:7	329:4 362:20	100:18,21	419:6,14,18
236:19 239:13	458:18	363:5 382:19	102:2,4 109:1	420:17 422:2
246:17 254:2	susan.sharko...	409:22 420:13	116:9 120:7,8	423:13 425:14
258:16 267:13	3:10	432:14 442:23	122:11 123:6	425:24 430:18
280:24 281:20	sworn 11:20	492:15	125:5 128:10	431:17 432:1,9
304:20 309:6,8	517:5 520:19	Taher's 227:7	129:15 130:2,7	432:12,19
317:1,6 318:7	system 173:11	230:14	130:17 131:18	433:11 435:5
320:18 324:23	487:13	take 26:4,13	132:7,9,18	435:14 436:13
328:14 333:18	systematic 8:18	27:6 34:20	134:3,10,20,21	436:14,21
335:22 349:8	94:10,13	37:16 40:18	138:1,5,10	437:3 438:6
349:16 360:9	289:11 304:5	79:23 97:14	142:8,14 149:9	439:4,6,15,22
365:19 377:1	304:21 305:1	125:19,24	153:4 165:2,22	440:8,18 441:6
387:23 390:14	systematically	126:5 138:4,13	170:9 175:19	441:21 442:14
399:15 406:20	94:6	168:5 179:24	176:7 180:12	444:11,12
409:19 412:16	Systemic 6:21	202:22 221:14	182:2,8 189:19	445:11,14,22
413:3,7 420:8		223:22 225:22	220:24 228:20	445:23 446:6
421:6 422:6,10	T	226:4 234:21	237:22 241:6	447:19 448:10
438:7 441:10	T 5:10 6:2 7:2	263:9 269:21	245:6 246:15	448:15 450:22
442:5 452:23	8:2 9:2 519:1	295:2 321:3	246:20 248:15	464:17,24

465:23 466:5,9	345:18 346:14	329:19,23,24	475:12,13	text 286:14
467:23 469:9	347:3 353:16	340:9 353:21	tend 179:3 250:4	287:7,14,21
469:15 470:7	353:23 367:15	361:4 363:3	term 33:16 39:8	textbooks 287:3
472:21 474:4	384:21 391:3	380:14,24	149:16 177:10	thank 12:19
475:20 476:16	394:3 404:6,16	381:13 395:4	177:11 197:19	14:21 24:16
478:18 482:13	408:5 409:20	400:21 409:14	255:2 269:1,6	28:16 47:22
482:16,23	422:20 423:13	430:4 456:22	269:7 296:9	52:19 56:20
483:13,24	427:17 442:7	458:8 465:20	303:19 359:6,9	58:1 70:6
484:24 485:12	447:20,23	478:5 505:18	359:23 371:22	71:15 80:13
487:20 496:5	478:10,11,16	tasked 92:18	375:11 407:12	81:23 85:11
503:8,15,20,22	478:22 479:2,5	taught 284:11	475:11	86:19 96:4
505:2,11	479:22 480:23	294:19	terms 120:6	102:10 114:19
507:12,19	481:21 482:11	teach 306:7,8	362:16	119:11 133:19
508:4,11	482:15 483:12	teaching 288:7	Terry 135:12	141:9 162:6
509:21 510:5	487:15 491:3	team 153:20	409:7,7	170:3 180:23
510:15 512:13	491:13,16	TECHNICIAN	test 79:17	184:22 199:9
512:15 513:2	492:20 496:15	4:9	236:13 269:9	200:18 213:19
talcum 1:5	497:21 499:5	teeth 250:20	477:8 497:15	220:13 223:13
11:11 13:1,10	503:16 504:14	tell 15:7 35:22	499:6 504:8	239:24 241:1
16:12 22:3,7	505:4 507:22	68:22 79:1	testified 11:21	283:7 296:6
22:12,20 23:1	508:14 510:17	118:16 132:3	12:24 13:5,9	315:21 368:8
27:8 28:23	512:19 514:9	140:20 141:1	13:19 47:23	430:12 440:3
29:5,9,13,18	515:8,13	148:17 212:9	93:4 96:16	465:15 472:17
30:5 31:16	talk 21:23 92:11	234:8 292:12	332:22 333:7	515:21
33:1,5 34:21	173:18 198:20	295:19 297:5	354:23 386:13	thanks 59:13
35:12,23 36:13	202:3 235:1	315:11 342:7	testify 39:3	283:8 298:13
36:19 37:11,23	308:23 309:1,3	359:21 368:22	61:21 145:1	470:2
38:18 44:15	309:14,18	405:14 407:8	346:11	theme 66:24
84:7,12 96:9	323:2 337:12	421:1,2 451:17	testifying 15:10	theories 57:5
96:10,22,23	363:13 383:12	455:22,23	42:16 88:1	59:2
98:5 103:18	390:10 406:18	478:4 479:10	346:21	theory 433:13
108:17,24	409:17 410:2	479:20 484:7	testimony 5:4	433:16 445:18
109:4,13,22	440:4 452:10	498:23 500:23	39:17 42:11	therapy 205:18
113:17 115:6	talked 88:14	501:24 506:17	45:24 46:10	242:22
124:9 145:3,7	346:23 414:22	telling 51:13	52:23 59:24	thing 26:19 73:9
145:14 154:15	talking 15:18	70:14 166:21	62:14 64:18,20	83:7 122:19
170:7 174:2,14	81:6,9 82:23	231:19 362:24	65:14 66:1,2	130:5 137:23
174:22 175:1,6	82:24 83:8	482:4 490:24	71:24 82:7,14	184:16 218:16
175:9,15	85:3,4,5,7,8	509:4 512:14	104:9 130:14	227:15 236:24
224:20 245:16	86:22 135:19	513:1	165:5 283:5	237:1 260:9
248:2 252:9	139:3 167:18	ten 361:16	372:23 450:17	263:12 264:5
253:18 254:4	206:7,10	364:17 368:15	478:21 509:20	277:5 294:20
267:4 309:24	208:14 221:10	373:2 385:2	515:4 517:6	319:12,18
310:20 311:11	231:15,17	387:20 389:6	testing 170:7	323:1 328:17
316:3 336:13	242:24,24	472:21,22	478:9,16,22	338:22 339:20
336:18,22	272:12 309:12	474:11,18,19	498:2 499:4	361:10 373:12
337:14 344:11	313:4 329:15	474:24 475:2,2	tests 18:16	388:17 449:6

461:18 464:1	194:20 196:13	493:9	21:9 35:4 44:6	233:22,24
474:13 479:18	198:17 206:2	thinks 229:16	48:21 60:1,23	289:15 345:4
506:3	213:21 215:21	399:22	61:6 69:11	471:13 502:17
things 20:16	221:9 223:8,9	third 258:24	79:12,15,22	tissue 123:7
36:23 66:15	248:8 249:9	462:20,23,24	125:21 126:10	389:14 390:9
77:11 98:11	250:16,23	thirty 518:16	126:15 137:10	390:21 391:19
137:11 157:22	251:17 252:3	THOMPSON	164:3,17	393:4 398:21
189:21 205:19	252:14,23	2:13	171:16 181:3,3	399:17 431:19
237:4 251:18	254:20 262:7	thorough 27:1	195:22 201:18	449:22 462:3
251:19,22	262:17 263:18	90:18	202:22 212:7	465:2
276:24 277:4	263:18 264:4	thought 27:20	217:24 228:9	title 74:11,11
277:10 278:3,8	264:19 265:8	30:24 31:4	229:16 239:11	121:19 200:20
284:4 285:5	266:11,13,21	44:1 78:21	239:15,19	203:17 467:22
290:11 295:7	274:16 282:17	116:1 125:17	248:17 254:12	487:1
314:18 315:2,3	283:19 286:9	138:18 144:15	262:14,20	titled 71:10
315:23 320:3	290:19 291:16	282:5 283:24	264:11,13,24	110:14 134:9
323:13 324:7	292:1 297:6	285:16 294:14	266:8 268:20	180:12 292:22
326:12 332:12	307:16 319:20	294:17 314:22	269:3,18,21	302:17 488:16
342:20 388:20	319:22 323:20	320:4 328:13	270:11,19	503:7
399:7 402:20	335:8 338:8,23	354:10 371:16	286:2 289:17	today 11:12
402:21 437:1	353:3 356:10	371:24 404:20	295:6 316:16	12:20 16:13
449:20 463:11	360:21 364:24	414:9,11	319:4 326:8,9	37:16 46:1,10
495:8 499:18	369:9,15	416:13 465:12	336:6 338:19	49:4 59:12
499:23	370:12,16	501:12	339:2 343:18	60:21 61:12
think 16:4 19:6	371:13 372:15	thousands 506:9	343:22 344:12	62:12,21 65:15
20:18 21:5	375:16 379:22	three 13:18	345:3 348:11	65:21 67:1
24:15 26:19	380:23 382:3,5	73:18 81:9	348:15 352:24	69:3 76:20
27:22 31:19	382:5,11 388:8	87:7 93:14	353:2 361:4,19	77:9 102:20
33:15 34:3	393:2,21	131:14 229:3	364:16 366:9	112:21 113:3
38:5,8,13	394:18 396:10	233:10 290:16	366:12 381:17	113:16 123:16
42:14 46:6	397:7 398:6,11	296:9 305:7	403:10 409:14	151:7 342:24
53:18,23 63:11	402:22 408:23	311:17 318:17	419:13 421:3	371:7,17
63:23 65:19	409:7 429:16	328:2 329:1	421:11,16,16	463:24 464:12
66:6,24 68:10	435:1 449:19	352:19 389:17	421:20 431:5,7	471:13 492:12
68:16 69:6,23	458:6 462:12	410:4 417:6	431:12 433:4	496:13
70:9,16 77:6,8	464:10 465:9	453:20 464:7	450:24 452:1	today's 11:6
78:3,4 80:6,24	470:4 473:14	493:12	453:9,12	56:21 59:8,16
81:1 82:7 83:3	473:15 475:5	threshold	462:20,23	60:3 102:19
83:10 100:2	476:5 477:2	202:17	463:1 473:10	113:2 114:16
110:9 129:20	480:16 485:21	thresholds	473:23 474:16	516:4
135:24 137:21	498:5,10	204:5	481:14 486:2,6	told 91:14 118:2
138:4,7 140:18	499:20 500:4	throw 40:16	493:10,24	260:7 371:8,16
149:9 151:10	501:18 502:7	232:8,10 233:4	494:3 506:8,15	389:15 402:22
156:13 158:5	505:23 506:1,3	236:14 294:23	516:5	495:9 501:21
164:20 168:14	514:19	throwing 235:22	times 13:17,20	505:11 510:16
177:9,17 184:4	thinking 27:18	time 11:7 12:24	16:3 50:18	toothpaste
190:2,20 192:9	293:12 360:13	14:22,24 19:24	66:20 67:15	250:21

top 74:13 141:21 196:1 270:23 304:4,18 319:17 334:20 350:24 357:14 430:4 441:15 469:23 497:7 topic 60:24 62:6 62:7 92:20 128:7 152:20 206:17 209:22 224:10 253:17 262:13 264:9,9 325:1 389:21 459:6 total 113:14 368:16 386:2 417:1 totality 48:18 49:4,10 54:22 114:14 116:8 137:6 162:9,14 289:7 307:11 336:20 352:7 402:19 481:12 481:21 483:16 484:6,12 511:22 totally 94:17 208:8 390:17 tough 176:12 493:6 TPP 8:20,21 Trabert 454:15 tract 173:11 423:1 427:6 437:20,24 438:15 444:11 445:15 448:9 train 328:13 trained 284:3,8 transcript 5:14 5:17,19 39:24 40:22 41:11 45:10,12 65:18 68:15 517:9,19 518:17,19	transcription 520:7 transcripts 54:6 transform 19:11 transformation 451:1 transformed 433:17 translocate 422:2,20 423:14 438:7 translocation 429:8 436:21 transport 432:7 437:9,16 transports 437:6 travel 438:15 travels 134:22 treat 206:12 213:22 treated 469:15 treatise 194:13 194:17 treatment 13:15 14:14 trend 268:19,23 269:2,6 trial 13:6,10 37:19 116:16 228:21 453:20 trials 101:2 293:22 305:9 tried 115:24 204:15 263:11 trouble 75:6 215:17 true 13:3,4 14:16 17:1 22:5,10,11,14 22:18,22 23:24 24:23 33:3 36:22,23 37:14 44:13,22 49:16 49:19 50:9 59:6 60:7,11 88:2 102:6	111:24 124:22 125:7 140:7,8 161:6 171:5,15 193:22 221:16 237:23 257:23 309:17 312:18 315:14,19,20 316:1,14,15 317:11 332:24 341:7 343:7,14 344:14 349:10 349:14,15,19 352:3,4 355:11 360:6 364:8 367:16,18 371:4 383:10 388:23 413:12 413:15 429:6 432:4 439:24 440:1 443:10 458:18,18 464:14 487:21 517:6 trust 179:3,9,14 179:19 386:24 trusting 178:22 truth 15:7 154:14 238:23 361:24 399:10 509:4 511:21 try 15:21 122:9 122:23 212:7 274:23 295:6 297:22 353:12 trying 14:6 46:19 68:17,22 69:2 70:16 95:7,7 123:10 140:18 159:4 274:14 295:13 297:24 313:3 328:3,13 338:20 340:12 400:17 417:9 418:3 438:11 460:9,10 463:8 463:9 472:24	tubal 441:23 442:8,16 443:5 444:8,19 446:5 tube 452:8 tubes 422:4,21 423:15 438:17 441:22 443:21 tubular 448:19 TUCKER 4:2 tumor 390:21 448:22 450:12 450:23 tumors 409:2 461:12 turn 41:11 64:22 72:3 84:23 87:2,5 111:13 116:11 133:15 134:7 135:7 186:3 202:19 256:5 258:22 271:14 273:21 275:13 281:2 334:3 359:8 367:21 407:3 420:9 424:22 430:3,12 443:17 446:10 458:22 471:14 471:15 482:8 486:19 turning 85:12 216:24 217:9 224:9,10 384:19 TV 264:12 twice 139:1 175:10 250:20 251:1 356:11 two 48:11 73:15 79:2 89:4 94:18 118:21 122:24 140:19 192:10 193:6 201:20 203:2 296:10 301:1 305:7 320:10	321:5 322:9 328:6 332:12 355:16 364:21 366:4 373:6 380:6,9,22 381:1,5,6,6,18 381:22 391:11 407:13 445:13 449:19 455:2 457:24,24 470:19 471:5 474:20,24 475:4,12 476:6 489:23 two-sided 343:3 tying 98:10 Tylenol 456:1,2 type 6:15 21:21 28:1,12 56:6 244:3 249:19 250:2 259:10 259:13,14 260:12,14,22 261:1 272:13 272:15 308:13 353:20 354:8 354:24 355:2 408:11 461:12 461:14 types 42:13 74:8 75:16 76:3 85:17 94:18 259:16,22 282:2 324:18 typically 15:2 18:3 118:20 222:8 262:3
--	---	---	---	--

U

U.S 365:24,24

366:2

umbrella 21:17**un-peer-revie...**

443:8,12

unable 361:14**unartful** 16:2**unclear** 85:5

underlying 50:10	unfortunately 179:8 388:16 471:16	248:2,8 250:5 250:6,24 256:22 257:1,9	289:19 290:3 292:8	470:2 473:9,22 486:1,5 516:2
understand 15:8 15:13 16:1,14 24:18 29:8,12 29:17 30:2,6 37:15,20 52:6 52:10 54:17 69:3 85:24 86:14,16 90:11 94:18 101:3 103:5 105:2 107:4,9 140:10 144:19 146:13 154:10,18 155:1,6,17 161:16,22 167:10 173:19 195:3,13 197:7 209:2 215:6 234:19 250:14 251:6,13 252:19 258:19 279:11 295:1 297:24 298:11 298:12 301:21 324:8 365:4,14 401:19 418:8 418:11 436:24 473:1 475:16 494:22 502:18	unimpressive 460:23 uninformed 156:13 Union 4:6 unique 303:1 United 1:1 29:17 30:4 32:13 145:1 154:11 240:13,15 248:1 249:1 universe 45:20 46:22 47:19 49:7 unnatural 438:22 unpublished 443:7,11,15 446:2 unreliable 188:1 188:12 191:16 191:24 252:8 unusually 335:2 335:8 unwarranted 217:13 update 149:13 150:24 usage 266:18 use 6:23 7:9,12 8:7,12,14,17 9:13 16:18 30:9 33:5 35:23 37:8 44:3 53:21 56:24 75:8 101:4 124:9 128:19 132:8 149:16 157:10 165:2 177:10 177:11 179:13 188:19 205:19 207:15 236:19 242:21 243:16	258:4 259:6 267:5 272:4 276:10,14 280:16 316:4 333:20 339:19 344:17,17,24 345:10 347:3 347:10,14,20 347:22 348:20 348:21 351:20 353:16,21,23 354:7 359:6,12 360:3 361:22 366:19 367:2 367:14 368:1 369:18 370:3,6 374:15 376:9 376:13,18 378:11,19 380:3 389:5,16 413:11 416:5 417:1,3,4,21 418:19 425:8 448:9 453:16 453:23 454:2 454:17 455:19 455:22 456:9 456:15 459:17 459:17 464:9 469:9 472:21 474:4,19,19 475:20 476:16 479:5 480:2 481:1,18 482:3 482:14 487:15 498:24 500:12 507:21 510:3 users 374:17 405:7 uses 29:5 225:17 248:14 480:8 usually 222:8 335:9 444:9 utility 287:20,22	V vacuum 375:23 vagina 128:15 130:12 425:17 438:16 vaginal 151:19 valid 178:9 179:16,22,24 236:15 368:9,9 368:13 371:1 372:4 373:12 validity 293:22 387:13 Valley 7:7 value 196:10 values 303:1 320:2 vanity 299:23 variety 274:7,12 275:2 316:13 vary 259:13 venued 14:10 verdict 266:10 515:6 version 148:11 185:10 472:7,9 versus 34:8 202:4 257:1,9 259:6 267:23 269:10 276:12 276:13 277:23 368:2 371:12 vicinity 408:14 victim 336:11 353:5 Victor 468:24 videographer 11:2,4 126:9 126:14 239:14 239:18 343:17 343:21 348:7 348:14 421:15 421:19 453:9 453:12 469:22	VIDEOTAPE 4:9 videotaped 1:13 6:6 11:8 view 164:5 violation 154:24 virus 120:15 vitro 153:15,18 voice 57:22 240:22 voicing 411:9 Volume 5:23 71:10 vulva 128:9
understanding 38:20 41:16,24 42:7,12 43:8 43:10,19 46:18 91:6 92:15 178:21,24 251:17 314:1 345:5 366:24 422:7 understood 16:7 190:12 underwear 336:13 unethical 439:7 unexposed 397:13 398:22			W W 4:3 Wacker 4:3 wait 15:22 465:14 waiting 15:21 169:23 want 15:18 16:3 16:9 24:17 47:11,14 72:24 76:7 81:16 84:17 92:12 125:23 126:4 129:16,19 141:18 162:11 168:8 211:21 211:24 212:9 216:17,22 218:10 219:18 219:23 220:1 222:1 258:13 258:18 274:20 297:11 320:18 328:14 334:14 337:14 354:14 380:7 390:18 396:22 400:13 401:21 402:19 422:6 453:1 467:7 471:23	

472:12 474:15	72:6 101:13	81:13 102:17	302:5,16	18:13 19:3,21
479:2 480:7	163:6 178:5	117:22 125:20	welcome 169:13	20:21 24:3
482:10 483:5	193:1 215:22	139:21 169:8	well-designed	26:4 27:4,15
483:10 489:16	215:23 233:10	379:5 392:14	306:10	28:5 29:4,22
491:11 494:6	270:20 283:7	405:20 406:7,8	well-known	32:8,19 33:9
495:2 503:5	284:8 317:4	411:22 428:15	262:21	33:15 35:2,17
507:18 513:24	330:5 376:11	463:24 495:7	went 53:21 57:8	36:3 38:24
wanted 82:13	390:15 395:8	506:9	75:6 80:23	39:7 40:10
125:18 149:2	395:24 413:3	weak 165:7	314:19 350:10	42:5 43:24
149:14 150:2,9	435:24 445:22	222:10 247:3	350:11 352:1	44:21 46:4
152:17 169:15	460:10 506:16	476:14 479:14	356:9 369:19	48:8 49:19
342:3,5 413:4	ways 226:17	484:9	373:23 395:19	50:16 51:4,21
wants 73:13	284:23 455:12	weakened	435:13,18	53:6 55:24
250:22	457:11 458:22	390:12	454:7 457:23	58:2,10 60:7
War 63:9 69:8,9	458:24 459:7	weaker 479:13	458:22 461:9	60:18 62:2,19
69:9	459:16 471:2	479:16 484:8	498:3	63:2,23 70:14
warning 244:21	509:12	502:5	weren't 42:23	72:23 74:3
499:15,19	we'll 87:2,13,13	weakly 479:16	409:3	77:6 79:8
500:1,9,11,16	110:13 123:19	weakness	West 2:8	89:23 90:24
500:19,24	125:14 141:13	164:15 352:21	WHI 311:8	92:2,14 95:6
501:3,14,17	208:20,21	360:7 381:24	374:9 375:15	95:21 96:14
502:2,13,18	209:22 210:4,4	392:5	383:15	98:9 99:22
509:8	244:6 254:24	weaknesses 80:3	whichever 21:13	101:22 103:21
Washington	324:22 328:4	164:21 283:21	white 270:9	104:15 105:1
3:18	328:18 366:13	308:2,11	wide 316:13	106:10 108:14
wasn't 25:17	400:24 401:1	390:11 391:18	386:12,15,19	109:9,17
31:24 36:3	403:4,7 418:10	392:21,22	387:2	113:24 116:23
58:21 80:17	436:4	470:10	widely 196:3	117:9 118:1,20
88:11 122:24	we're 16:11	web 306:3	262:16 263:3,4	119:7 121:13
125:11 144:22	37:16 43:15	website 9:22	263:5,8,24	122:8,18
197:1 227:21	65:20 66:24	283:10,11,23	265:4,8 282:1	124:13 125:11
245:1 260:8	76:20 77:8	302:16 303:10	287:6,16	126:2,6 127:11
261:13 288:14	84:18 98:10	306:4,15 497:3	wider 386:9	127:22 130:22
291:7 314:5	99:12 125:12	503:7,14,19	widespread	132:1 133:13
330:23 353:11	139:4 168:6	507:15	122:21 272:2,7	136:15 137:4
371:20 379:7	169:10 189:11	week 81:1,1	278:13 279:21	140:1 141:18
393:15 408:22	189:12 206:7	111:12,12	Wilson 462:1,10	142:5,18 143:5
409:10 412:24	206:10 209:21	143:17 345:1,3	462:18 463:18	146:8 147:13
434:18 465:5	243:1 270:17	345:4 368:2,2	wish 285:23	150:19 152:9
478:24 510:10	311:2 321:22	370:7 373:5,14	withdraw	153:10 155:4
waste 203:4	324:21 334:16	weeks 140:19	159:19 199:6	156:5,16
wasted 431:6	360:8 363:6,7	Wehner 134:12	358:7 384:18	157:19 159:3
watch 361:11	389:18 390:3	weigh 158:24	415:6	160:22 161:9
403:2 472:2	396:4 397:10	311:18	withdrawn	163:2,14,24
water 196:5	409:16 458:6,7	Weil 1:14 3:12	169:1,13	166:4,11,14
way 14:1 23:15	511:13 515:24	Weill 7:18 12:17	witness 10:5	168:16 170:18
25:8 39:12	we've 15:3 68:23	301:2,20,23	17:1,14 18:3	172:9,19 173:6

173:16 174:6	349:22 350:21	513:14 514:12	455:24	worry 361:3
175:23 176:11	355:14 356:22	514:18 515:22	women's 352:11	506:16
177:6,20 179:7	358:13 359:12	517:5,6,8	wonder 132:21	worth 382:10
185:4 191:1	360:18 362:12	518:1	166:24	worthwhile
192:5 193:14	364:14 365:1	Wolf 156:18	wondering	288:22 289:2
195:7 196:20	366:8 369:9	157:5	94:10	300:5 414:10
197:6 198:15	370:20 372:22	woman 243:18	word 16:19	wouldn't 36:4
203:15 207:3	375:22 377:9	352:17 389:7	24:21 119:12	132:22 173:9
208:9 211:7,17	379:22 381:9	389:16 439:14	171:6,18	177:11 219:20
213:7 215:11	383:1 385:8,21	456:5 498:16	179:11,13,14	226:8,12 236:9
216:8 218:6	386:8 387:17	woman's 174:3	183:7 255:10	330:6,13
219:12 221:23	388:8,16 391:9	338:18 438:1	309:11 335:9	386:24 388:13
223:6 230:12	393:9 394:10	438:15	406:16 425:4	401:4 402:17
231:6 232:21	394:16 395:17	women 28:23	433:19 477:4	412:19 439:8
234:18 235:9	397:17 398:5	29:8,13,17	508:5	439:18 495:17
235:15 237:17	399:21 400:5	30:8,15 31:15	wording 508:6	501:14,24
238:2,22	401:11 402:12	32:3,12 33:5	words 21:19	506:16 509:18
241:15 242:4	406:3 410:23	63:7 87:22	53:21 134:20	Wright 9:18
242:15 244:3	412:15,23	88:7,23 151:20	240:9 262:2	488:24 489:21
244:16 245:10	419:23 423:19	152:1 226:8,11	360:11 407:13	490:4
245:24 246:9	427:21 432:23	243:15 245:2	413:24 450:23	write 118:16
246:24 248:5	433:8 434:3,21	248:19 250:4	455:13 476:22	119:3 215:17
249:9,24	435:8 436:18	311:4 318:16	work 44:7,9	295:6 411:9
251:16 252:14	438:4 439:13	320:7,9 326:12	103:17 107:12	writing 77:20
253:4,23	440:13 441:13	330:16 338:2	112:2 113:1,8	118:22
254:11 257:14	442:2,12 447:6	339:9 340:13	113:12,16	written 22:24
257:23 260:2	448:5 451:7	340:18 341:6	140:12 141:5	118:8 426:15
262:10 265:7	452:23 453:14	345:18,23	142:8 153:23	426:18,19,21
267:10 268:15	454:23 458:15	351:19 356:6	154:1 288:7	426:23 488:23
273:2 276:4	458:19 460:5	364:2,4,10,12	300:23,24	wrong 83:11
277:20 278:18	462:7,15	364:15 365:5,6	301:1,12 389:2	157:22 158:1
279:4 282:13	464:22 469:4	365:24 368:15	389:3 391:2	205:14 217:2
286:18 288:2	470:17 472:10	368:20 369:4	460:17,18	275:23 309:13
289:1,23 291:6	476:1 477:22	369:18,23	461:17,17	322:16 386:19
295:19 296:4	478:21 480:7	370:2,6 373:4	490:18 504:6	426:6 427:11
296:24 299:2	481:4 482:20	373:7,22 382:9	504:22 515:3,8	wrote 185:8
300:20 302:3	484:21 485:6	383:16,23	worked 118:21	194:23 213:8
304:16 305:24	487:24 489:11	384:7,11,20,24	working 87:15	Wu 232:2,3
307:9 312:4,17	491:7,19 493:2	385:2,11,12,18	87:17 93:7	416:11,14,15
316:8,24	494:13 496:9	386:1,2 387:3	272:5 369:14	416:22,23,24
317:20 318:7	496:18 498:1	387:4,9,11,12	492:11	417:3,5,14,18
319:10 327:15	499:10 500:4	387:20 390:16	works 155:7	417:19 418:4,5
330:9 331:13	500:15,23	390:23,24	502:23	418:15,18,19
333:3 338:8	501:10 504:18	391:3,10,20	world 69:8,9	
340:22 341:10	506:23 508:1	397:3,8 404:2	483:8 494:10	X
343:14 344:21	508:18 510:20	404:3,5 405:3	worried 204:23	X 5:2,10 6:2 7:2
346:7,18 349:7	512:5,24	439:3 443:19	513:19	8:2 9:2

Y	384:8,12 385:2	148:3,6,7,8,18	358:2	429:21 430:6
yeah 24:13	387:20 389:6	148:21 150:12	100 5:23 234:2,4	503:11
35:17 72:10	404:23 448:15	186:4 190:18	235:5	1950s 30:10,17
73:3 83:17,22	451:2 461:5	192:9 204:11	100-C 71:10	31:18 32:5,15
114:5 126:6	466:15 467:12	219:6 240:3	100,300 113:14	306:22
127:16 129:10	467:20 472:21	269:13 281:1	102 6:6	1970s 30:11,18
133:13 141:19	472:22 474:11	328:5 347:19	103 5:20 64:22	31:18 32:16
186:16 193:4	474:18,19	461:14 491:14	103,000 114:6	1976 365:22
207:7 208:18	475:12,13	491:22 492:5	11 30:24 220:12	1982 240:9
219:20 229:22	years' 339:10	492:21 494:2,7	258:22 357:14	344:12 345:17
240:20,24	yeast 36:11,14	495:5 520:6	374:13,19	366:22 367:3
251:9 256:12	yesterday 81:8	1.02 353:18	375:6 428:16	1989 365:23
261:7 264:14	81:12 112:21	354:18 376:24	11:28 126:11	199 6:17
299:19 321:1	112:22	378:17	11:42 126:16	1996 48:4 432:3
328:12 329:22	York 1:14,15	1.06 207:16	110 6:7	1st 424:17 428:6
333:6 337:19	11:10,10 14:11	370:7	114 6:10	
340:14 349:12	301:6,17	1.09 348:4,22	116,430 366:2	2
377:4,9 385:15	younger 364:3	349:19	12 5:5 125:15	2 41:12 45:10,11
385:17 393:12	364:11,18	1.1 182:5	224:4 339:6	111:8 181:10
399:6 404:4	365:6 367:5	1.16 474:12,21	340:6,14 397:3	181:11,16,21
416:3 418:11		1.2 187:20	397:4 404:8,17	181:21 202:17
454:6 472:1,5	Z	245:11 318:2	12-risk 474:17	344:23 347:5,9
475:18 476:20	zero 198:22	1.22 408:14	121,700 365:24	347:9 350:3
499:16 507:16	202:21	1.24 244:12,22	13 147:20	384:20 386:23
510:12	Zervomanola...	271:4 409:24	255:19 407:10	415:20 442:23
year 6:15 363:23	437:19	1.28 271:4	407:14 453:19	443:1 461:12
376:9 389:7	ZIP 107:6	1.3 245:7 318:2	14 45:17 248:20	2-A 415:18,19
488:21 489:6		1.31 271:4	349:11,12	416:5
489:22	0	1.35 370:9	350:2,8,13	2-B 491:22
years 47:12	0.05 202:18	408:14	352:15 355:17	492:5 494:2
78:19 206:17	0.09 347:24	1.37 347:16	1416 275:13	495:5
228:23 229:2	0.84 370:8	348:23	1490 2:9	2.0 241:23
327:5,8 332:19	0.86 347:16	1.38 409:24	15 274:3 338:2	2/25/19 6:12
332:20,21	348:23	1.4 182:5 245:7	351:6 352:17	2:04 239:20
333:8,14 336:5	000489048-54	353:18 354:17	155 3:4	20 125:8 187:21
337:24 338:2,4	9:7	354:21 373:17	16 134:8,9	245:15 325:4,5
339:5,8 340:6	02210 3:4	1.6 187:20	292:22	328:21 332:19
340:14 350:2,8	07932 3:9	245:12	16-2738 1:6	332:21 333:8
350:13 351:6	08542 3:13	1.6.5 83:15	17 3:13 302:13	337:24 338:3
352:15,17,19		1.9 347:15	18 334:1 446:11	339:5,10
355:17,20	1	1.91 353:19	180 6:13	363:18 376:11
356:1,6 361:16	1 6:15 39:19	354:18 376:24	183 113:20	384:8,12
364:17 368:15	40:7,21 74:16	378:17	184,000 113:20	429:20 430:13
368:16 369:2	82:5 96:6,11	1:07 239:16	186 6:15	520:20
369:19 373:3,6	96:17,24 97:5	10 45:16 111:9	19 2:4 64:23	20-fold 392:10
376:10,10,11	97:12 98:7	187:18 200:4	160:9 344:8	200 346:3
	99:1,19 111:8	332:20 338:2	428:18 429:20	200,000 318:16

318:20 385:23 386:1,2 2000 344:2 358:10 359:20 363:24 411:18 440:24 462:18 20004 3:18 2002 69:24 2003 333:13 334:2 2007 135:2,4 139:13 465:22 2008 373:9,15 2009 139:13 232:3,4,6,7 416:24,24 417:5 418:6,15 418:18,20 201 3:13 2010 48:3,4 220:12 224:15 228:20 247:21 357:14 358:4 359:18 362:8 363:13,19,20 364:3,11 367:13 368:14 379:7,16 382:4 411:23 412:10 413:20 419:12 491:21 492:19 2012 48:5 69:17 70:4,10 71:9 83:14 86:15 95:3,19 96:7 2013 379:5 454:15 2014 254:18,19 264:24 265:4,9 276:12,12,13 277:22 278:15 279:6,22 280:6 377:20 424:17 428:6 2015 232:2,6 303:5 416:11 416:23 417:4	417:18,19 418:4,19 462:2 463:18 2016 180:14 232:4,7 249:4 254:15 255:8 259:8 260:6 275:3 329:11 338:24 446:20 2017 38:6 2018 6:20 38:9 40:22 43:6 45:14 64:20 142:15 143:12 145:17 146:2 224:3 259:11 259:12 360:3 420:13 432:14 442:23 454:11 2019 1:10 11:7 49:14 104:12 108:5 111:16 115:3 124:6,7 124:19,20 125:3 139:20 147:2,20 151:4 200:8 432:17 433:2 434:13 486:11 491:21 503:11 517:15 202 3:19 20s 339:1 340:11 21 200:8 378:1,2 420:10 428:18 430:6,13 218 2:14 219 72:4,9,13,15 72:21 74:5 76:23 82:5 85:12 21st 200:7 22 126:18 127:4 403:20 220 6:19 224 6:21 23 140:9 141:8,9 141:21 334:4	407:2 486:11 231 334:4,6,16 232 82:13,17,18 83:5 84:16 233 4:3 24 214:20 339:8 355:20 356:1 397:3 407:22 25 49:14 104:12 108:5 115:3 116:13 124:6 124:19 125:3 147:2 366:3 424:15 250 214:19 251 350:15 351:1,12 255 7:6 256 87:10 93:5 25th 51:18 110:10 111:15 26 368:16 468:12,14 269-2343 2:15 27 1:10 11:6 311:16 471:12 271 7:9 273 7:12 28 258:23 259:3 261:5 517:15 281 7:16 29 488:9 292 7:18 <hr/> 3 3 64:12 103:16 147:6,14,18 229:18,21 471:19,21,24 472:12 474:3 475:15,19 3:28 343:19 3:55 343:23 3:59 348:12 30 25:10,11,21 55:11 328:22 332:20 333:14	336:5 366:1 369:2 496:24 518:16 302 7:21 31 503:6 312 4:5 33 116:13 275:8 443:17 334 2:15 338-1100 2:10 344 8:6 356 87:5,8 358 271:15 36104 2:14 363 8:9 37 349:13 377 8:12 <hr/> 4 4 45:19 71:9 367:22 384:19 425:2 4/1/14 9:6 4:00 348:16 40 5:14 206:17 333:8,14 336:5 337:24 338:4 369:2 376:23 378:16 40,000 506:12 403 8:14 406 8:17 407 8:20 41,000 318:19 404:3 41,654 404:2 42 248:19 366:3 424 9:6 43 416:17 439-2286 3:5 45 5:16 46 415:15,20,22 463-2400 3:19 464 256:4 468 9:8 471 9:13 486 9:15	488 9:17 49 224:11,13 496 9:19 <hr/> 5 5 102:12,18 146:19,23 147:17 229:18 229:21 424:23 425:2,2 5/7/18 5:15,17 5:20 5:01 421:16 5:22 421:21 5:49 453:10,13 50 248:24 249:6 340:13 341:24 367:24 50/50 150:8,10 236:2,2,3 273:18 392:18 479:18 501 2:8 503 9:22 50s 32:21 521 520:6 549-7000 3:9 55 338:19 366:1 56 5:15 41:11 57 5:18 45:16 <hr/> 6 6 110:8 121:8 146:12,20 6.2 420:10 6.4 258:24 6.6 404:23 6:03 473:10 6:04 473:24 6:13 486:2 6:36 486:7 6:59 516:5,8 60 187:21 245:15 60,000 506:11 600 3:8 404:3 60606 4:4
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Kevin Holcomb, M.D.

Page 579

609 3:14	9			
60s 30:10,17	9 111:8 186:5			
31:18 32:5,15	269:20 274:4			
32:21	274:10			
61 44:16 45:18	9:53 1:15 11:7			
46:24 47:17	90 59:23 60:4			
106:6 116:15	354:4 371:2			
61,000 318:18	917.591.5672			
375:16 387:11	1:20			
61,576 383:16	92101 2:9			
617 3:5	92660 2:4			
619 2:10	949 2:5			
624-6307 4:5	95 112:1 149:23			
64 5:19	187:4,4 193:21			
68 385:4,16	193:23 194:8			
386:3 387:12	196:13,22			
387:21	197:14 202:5			
69 229:19,21	205:20 371:3			
6950 4:4	372:8 378:16			
7	973 3:9			
7 45:14 64:20,23	975 3:18			
115:1	986-1118 3:14			
70 25:5,9 444:18	99 290:14			
70,000 506:11	318:21 329:2			
70s 32:6	440:24			
71 5:21				
720-1288 2:5				
767 1:14 11:9				
78,000 318:18				
78,630 345:23				
791 217:3				
7th 40:22				
8				
8 41:12 111:8				
180:9 281:1				
80,750 112:7				
114:9				
800 201:9				
203:12 214:20				
800-some 218:3				
850 60:9 112:4				
86 378:20				
877.370.3377				
1:20				
89 354:3				

Exhibit 9

1 UNITED STATES DISTRICT COURT
2 FOR THE DISTRICT OF NEW JERSEY
3
4 IN RE JOHNSON & JOHNSON TALCUM)
POWDER PRODUCTS MARKETING,)
5 SALES PRACTICES, AND PRODUCTS)
LIABILITY LITIGATION,)
6)MDL NO.
)16-2738(FLW)(LGH)
7 THIS DOCUMENT RELATES TO ALL)
CASES,)
8)
9
10
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12
13

14 VIDEOTAPED DEPOSITION OF CHERYL SAENZ, M.D.
15 SAN DIEGO, CALIFORNIA
16 WEDNESDAY, MARCH 13, 2019
17
18
19
20
21
22

23 STENOGRAPHICALLY REPORTED BY:
24

Valerie C. Rodriguez
25 CSR No. 12871 (orig 6980)

Cheryl Saenz, M.D.
86538

Page 2	Page 4
<p>1 UNITED STATES DISTRICT COURT</p> <p>2 FOR THE DISTRICT OF NEW JERSEY</p> <p>3</p> <p>4 IN RE JOHNSON & JOHNSON TALCUM)</p> <p>5 POWDER PRODUCTS MARKETING,)</p> <p>6 SALES PRACTICES, AND PRODUCTS)</p> <p>7 LIABILITY LITIGATION,)</p> <p>8)MDL NO.</p> <p>9)16-2738(FLW)(LGH)</p> <p>10 THIS DOCUMENT RELATES TO ALL)</p> <p>11 CASES,)</p> <p>12)</p> <p>13</p> <p>14</p> <p>15 VIDEOTAPED DEPOSITION OF CHERYL SAENZ, M D., TAKEN</p> <p>16 ON BEHALF OF THE DEFENDANTS, AT 12255 EL CAMINO</p> <p>17 REAL, STE. 100, SAN DIEGO, CALIFORNIA, COMMENCING AT</p> <p>18 9:30 a.m. AND ENDING AT 6:19 p.m. ON WEDNESDAY,</p> <p>19 MARCH 13, 2019, BEFORE VALERIE C. RODRIGUEZ,</p> <p>20 CERTIFIED SHORTHAND REPORTER NO. 12871 (ORIGINALLY</p> <p>21 6980).</p> <p>22</p> <p>23</p> <p>24</p> <p>25</p>	<p>1 APPEARANCES CONTINUED:</p> <p>2</p> <p>3</p> <p>4 FOR DEFENDANTS JOHNSON & JOHNSON</p> <p>5 DRINKER, BIDDLE & REATH, LLP</p> <p>6 BY: SUSAN M. SHARKO, ESQ.</p> <p>7 600 CAMPUS DRIVE</p> <p>8 FLORHAM PARK, NEW JERSEY 07392</p> <p>9 973.549.7000</p> <p>10 SUSAN.SHARKO@DBR.COM</p> <p>11</p> <p>12 FOR DEFENDANT PTI ROYSTON/PTI</p> <p>13 TUCKER ELLIS LLP</p> <p>14 BY: MICHAEL ANDERTON, ESQ.</p> <p>15 950 MAIN AVENUE</p> <p>16 SUITE 1100</p> <p>17 CLEVELAND, OHIO 44113</p> <p>18 216.696.4835</p> <p>19 MICHAEL.ANDERTON@TUCKERELLIS.COM</p> <p>20 FOR DEFENDANTS PCPC:</p> <p>21 SEYFARTH SHAW LLP</p> <p>22 BY: RENEE B. APPEL, ESQ.</p> <p>23 975 F STREET, NW</p> <p>24 WASHINGTON, DC 20004-1454</p> <p>25 202.463.2400</p> <p>RAPPEL@SEYFARTH.COM</p> <p>ALSO PRESENT:</p> <p>DARNELL BROWN, VIDEOGRAPHER</p>
Page 3	Page 5
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Page 6		
1	INDEX OF EXHIBITS CONTINUED	
2	MARKED DESCRIPTION	PAGE
3	Exhibit 8 Videotaped Deposition	
4	Transcript of Rebecca	
5	Smith-Bindman, M.D. San	
6	Francisco, California	
7	Friday, February 8, 2019,	
8	Volume II	121
9	Exhibit 9 LB-044 - Talcum Powder	
10	Enhances Cancer	
11	Antigen 125 Levels in Ovarian	
12	Cancer Cells	
13	and in Normal Ovarian	
14	Epithelial Cells	142
15	Exhibit 10 214A Reproductive Sciences	
16	Vol. 25, Supplement 1, March	
17	2018 Scientific Abstracts	144
18	Exhibit 11 Biologic Plausibility:	
19	Migration/Translocation	194
20	Exhibit 12 Perineal Use of Talc and Risk	
21	of Ovarian Cancer	
22	H Langseth, 1 S E Hankinson,	
23	2 J Siemiatycki, 3 E	
24	Weiderpass 1A,5	204
25	Exhibit 13 Factors Related to	
	Inflammation of the Ovarian	
	Epithelium and Risk of	
	Ovarian Cancer by Roberta B.	
	Ness, 1 Jeane Ann Grisso, 2	
	Carrie Cottreau, 1 Jennifer	
	Klapper, 1 Ron Vergona, 1	
	James E. Wheeler, 3 Mark	
	Morgan, 4 and James J.	
	Schlesselman 5	207
	Exhibit 14 12871-6980	
	ACOG COMMITTEE OPINION	
	Number 374, August 2007	
	Reaffirmed 2016 Committee on	
	Ethics "Expert Testimony"	222

Page 7		
1	INDEX OF EXHIBITS CONTINUED	
2	MARKED DESCRIPTION	PAGE
3	Exhibit 15 Letter dated April 1st, 2014,	
4	Sent from the FDA to Samuel	
5	Epstein, MD	224
6	Exhibit 16 Fax from Richard Zazenski to	
7	Bill Ashton dated September	
8	30, 2004	226
9	Exhibit 17 REVIEW-Possible Role of	
10	Ovarian Epithelial	
11	Inflammation in Ovarian	
12	Cancer by Roberta B. Ness,	
13	Carrie Cottreau	232
14	Exhibit 18 Biologic Plausibility:	
15	Chronic Inflammation	242
16	Exhibit 19 Draft Screening Assessment	
17	Talc (Mg3H2(SiO3)4)	
18	Chemical Abstracts Service	
19	Registry Number 14807-96-6	
20	Environment and Climate	
21	Change Canada - Health Canada	246
22	Exhibit 20 NIH Public Access, Author	
23	Manuscript Published in final	
24	edited form as: Cancer	
25	Epidemiol Biomarkers Prev.	
	2008 September; 17(9):	
	2436-2444. Doi:	
	10.1158/1055-9965.EPI-08-0399	
	Talc use, variants of the	
	GSTM1, GSTT1, and NAT2 Genes,	
	and Risk of Epithelial	
	Ovarian Cancer	252
	Exhibit 21 © 2004 Wiley-Liss, Inc.	
	Publication of the	
	International Union Against	
	Cancer PERINEAL TALC EXPOSURE	
	AND EPITHELIAL OVARIAN CANCER	
	RISK IN THE CENTRAL VALLEY OF	
	CALIFORNIA	253

Page 8		
1	INDEX OF EXHIBITS CONTINUED	
2	MARKED DESCRIPTION	PAGE
3	Exhibit 22 RESEARCH ARTICLE -	
4	Associations Between Aspirin	
5	Use and the Risk of Cancers:	
6	A Meta-Analysis of	
7	Observational Studies By	
8	Yan Qiao Li, Tingting Yang 2),	
9	Yong Gan 1, Wenzhen Li 1, Chao	
10	Wang 1, Yanhong Gong 1 and	
11	Zuxun Lul	268
12	Exhibit 23 Aspirin, Nonaspirin	
13	Nonsteroidal	
14	Anti-Inflammatory Drug, and	
15	Acetaminophen Use and Risk of	
16	Invasive Epithelial Ovarian	
17	Cancer: A Pooled Analysis in	
18	the Ovarian Cancer	
19	Association Consortium by	
20	Britton Trabert	270
21	Exhibit 24 Expert report by Cheryl	
22	Saenz, MD, in the Echeverria	
23	matter	279
24	Exhibit 25 Genital Use of Talc and Risk	
25	of Ovarian Cancer: A	
	Meta-Analysis, by Wera Berge,	
	Kenneth Mundt, Hung Luu and	
	Paolo Boffetta	282
	Exhibit 26 [Review Article:	
	Gynecological Cancer]	
	Genital use of talc and risk	
	of ovarian cancer: A	
	meta-analysis by Berge, Wera;	
	Mundt, Kenneth; Luu, Hungc;	
	Boffetta, Paolo	286

Page 9		
1	INDEX OF EXHIBITS CONTINUED	
2	MARKED DESCRIPTION	PAGE
3	Exhibit 27 The Association Between Talc	
4	Use and Ovarian Cancer	
5	A Retrospective Case-Control	
6	Study in Two US States	
7	Daniel W Cramer, Allison F.	
8	Vitonis, Kathryn L. Terry,	
9	a,b William R. Welch, c and	
10	Linda J. Titusd	290
11	Exhibit 28 Genital powder use and risk	
12	of ovarian cancer: A pooled	
13	analysis of 8,525 cases and	
14	9,859 controls by Kathryn L.	
15	Terry	297
16	Exhibit 29 Systematic Review and	
17	Meta-Analysis of the	
18	Association between Perineal	
19	Use of Talc and Risk of	
20	Ovarian Cancer by Mohamed	
21	Kadry Taher	309
22	Exhibit 30 Clinical commentary Talc and	
23	ovarian cancer by Steven A.	
24	Narod	317
25	Exhibit 31 Perineal Talc Use and Ovarian	
	Cancer, A Systematic Review	
	and Meta-Analysis by	
	Ross Penninkilampi, and Guy	
	D. Eslick	322
	Exhibit 32 Prospective Study of Talc Use	
	and Ovarian Cancer by	
	Dorota M Gertig	324
	Exhibit 33 Risk Factors for Epithelial	
	Ovarian Cancer by Histologic	
	Subtype by Margaret A. Gates	325
	Exhibit 34 What Is New in Ovarian	
	Cancer? Best Articles From	
	the Past Year by Jason D.	
	Wright, MD	342

Cheryl Saenz, M.D.

<p style="text-align: right;">Page 10</p> <p>1 INDEX OF EXHIBITS CONTINUED</p> <p>2 MARKED DESCRIPTION PAGE</p> <p>3 Exhibit Arsenig, Metals, Fibres, and</p> <p>35 Dusts Volume 100 C, a Review</p> <p>4 of Human Carcinogens 346</p> <p>5 Exhibit Heller 1996 Asbestos Exposure</p> <p>36 and Ovarian Fiber Burden 350</p> <p>6</p> <p>7</p> <p>8 INFORMATION REQUESTED: (None)</p> <p>9</p> <p>10 DIRECTIONS NOT TO ANSWER: (None)</p> <p>11</p> <p>12</p> <p>13</p> <p>14</p> <p>15</p> <p>16</p> <p>17</p> <p>18</p> <p>19</p> <p>20</p> <p>21</p> <p>22</p> <p>23</p> <p>24</p> <p>25</p>	<p style="text-align: right;">Page 12</p> <p>1 MS. THOMPSON: Margaret Thompson on</p> <p>2 behalf of the plaintiffs.</p> <p>3 MS. BROWN: Paula Brown on behalf of the</p> <p>4 plaintiffs.</p> <p>5 VIDEOGRAPHER: The court reporter is</p> <p>6 Valerie Rodriguez who will now swear in the witness.</p> <p>7 CHERYL SAENZ, M.D.,</p> <p>8 having been first duly sworn,</p> <p>9 was examined and testified as follows:</p> <p>10</p> <p>11 EXAMINATION</p> <p>12 -o0o-</p> <p>13 BY MS. GARBER:</p> <p>14 Q Good morning.</p> <p>15 A Good morning.</p> <p>16 Q Will you state your name for the record.</p> <p>17 A Cheryl Christine Saenz.</p> <p>18 Q You're a medical doctor?</p> <p>19 A Yes.</p> <p>20 Q Dr. Saenz, we've had the occasion to meet</p> <p>21 before today, haven't we?</p> <p>22 A That's correct.</p> <p>23 Q And what is your memory of that meeting?</p> <p>24 MS. CURRY: Objection to form.</p> <p>25 THE WITNESS: I believe that you actually</p>
<p style="text-align: right;">Page 11</p> <p>1 SAN DIEGO, CALIFORNIA, WEDNESDAY, MARCH 13, 2019</p> <p>2 ~~~9:30 A.M.~~~</p> <p>3 -OOO-</p> <p>4</p> <p>5</p> <p>6 THE VIDEOGRAPHER: Good morning. We are</p> <p>7 now on the record. My name is Darnell Brown and I'm</p> <p>8 the videographer with Golkow Litigation Services.</p> <p>9 Today's date is March 13th, 2019, and the</p> <p>10 time is 9:29 a.m. This video deposition being is</p> <p>11 held in San Diego, California, in a matter of In Re:</p> <p>12 Talc, the United States district court for the</p> <p>13 district of New Jersey.</p> <p>14 The deponent is Dr. Cheryl Saenz.</p> <p>15 Counsel, please identify yourselves for the record.</p> <p>16 MS. CURRY: Dawn Curry on behalf of</p> <p>17 Johnson & Johnson.</p> <p>18 MS. SHARKO: Susan Sharko for Johnson &</p> <p>19 Johnson, the defendants.</p> <p>20 MR. ANDERTON: Michael Anderton for PTI</p> <p>21 Royston and PTI Union.</p> <p>22 MS. APPEL: Renee Appel on behalf of</p> <p>23 defendant Personal Care Products Council.</p> <p>24 MS. GARBER: Cynthia Garber on behalf of</p> <p>25 the plaintiffs.</p>	<p style="text-align: right;">Page 13</p> <p>1 took my deposition in a matter in 2017.</p> <p>2 BY MS. GARBER:</p> <p>3 Q That was in the Echeverria case; is that</p> <p>4 correct?</p> <p>5 A That's my recollection.</p> <p>6 Q That was in the California JCCP?</p> <p>7 A I don't know what you mean by that.</p> <p>8 Q That was venued in California in</p> <p>9 Los Angeles; is that correct?</p> <p>10 A Well, we took the deposition in</p> <p>11 San Diego, but I believe the case was tried in</p> <p>12 Los Angeles.</p> <p>13 Q Correct. You testified at that trial;</p> <p>14 did you not?</p> <p>15 A I did.</p> <p>16 Q You've testified at other talc product</p> <p>17 litigation cases, have you not?</p> <p>18 A Can you define for me what you mean by</p> <p>19 "testify"?</p> <p>20 Q Sure. Did you testify in court in</p> <p>21 connection with other talcum powder product cases</p> <p>22 aside from California?</p> <p>23 MS. CURRY: Object to the form.</p> <p>24 THE WITNESS: Only one other case.</p> <p>25 ///</p>

<p style="text-align: right;">Page 14</p> <p>1 BY MS. GARBER:</p> <p>2 Q What was the name of that case as you</p> <p>3 recall it?</p> <p>4 A My recollection is that that case was</p> <p>5 called Ingham, et al. versus Johnson & Johnson.</p> <p>6 Q Those are the only two occasions where</p> <p>7 you testified in court in connection with a talcum</p> <p>8 powder litigation?</p> <p>9 A That's correct.</p> <p>10 Q Do you hold yourself out as a gynecologic</p> <p>11 oncologist?</p> <p>12 A Well, I don't just hold myself out. I'm</p> <p>13 board certified in the subspecialty of gynecologic</p> <p>14 oncology, so I'm also recognized by the American</p> <p>15 Board of OB-GYN.</p> <p>16 Q And you're a medical doctor?</p> <p>17 A Yes.</p> <p>18 Q And you're licensed in the State of</p> <p>19 California to practice medicine?</p> <p>20 A Yes.</p> <p>21 Q You just mentioned you're board</p> <p>22 certification. So you're board certified by what's</p> <p>23 known as ACOG?</p> <p>24 A No.</p> <p>25 MS. CURRY: Object to the form.</p>	<p style="text-align: right;">Page 16</p> <p>1 MS. CURRY: Object to the form.</p> <p>2 THE WITNESS: I don't think that's quite</p> <p>3 accurate because that's not the way I look at it.</p> <p>4 I've testified at deposition twice in one matter,</p> <p>5 because initially, I was only offering testimony on</p> <p>6 six of the plaintiffs but then I gave additional</p> <p>7 testimony.</p> <p>8 So I still look at that as really only</p> <p>9 one deposition.</p> <p>10 BY MS. GARBER:</p> <p>11 Q Let me see if I can clarify. You've</p> <p>12 offered a deposition in connection with the</p> <p>13 Echeverria matter that you've already told us about;</p> <p>14 correct?</p> <p>15 A Correct.</p> <p>16 Q You've also provided deposition testimony</p> <p>17 in connection with the Ingham matter; correct?</p> <p>18 A Correct.</p> <p>19 Q You've also given deposition testimony in</p> <p>20 the Brower matter?</p> <p>21 A Correct.</p> <p>22 Q You've also given deposition testimony in</p> <p>23 the Forrest matter; correct?</p> <p>24 A Correct. So I apologize, you're correct.</p> <p>25 There are four.</p>
<p style="text-align: right;">Page 15</p> <p>1 BY MS. GARBER:</p> <p>2 Q I'm sorry. By the American board of</p> <p>3 obstetricians and gynecologists; correct?</p> <p>4 A Actually the board is called American</p> <p>5 Board of Obstetrics and Gynecology.</p> <p>6 Q Thank you. Are you a member of ACOG?</p> <p>7 A I am.</p> <p>8 Q You are also subspecialty board certified</p> <p>9 in gynecologic oncology?</p> <p>10 MS. CURRY: Object to the form.</p> <p>11 THE WITNESS: Right. So I actually hold</p> <p>12 two boards. I hold a board in obstetrics and</p> <p>13 gynecology and a board in gynecologic oncology.</p> <p>14 BY MS. GARBER:</p> <p>15 Q Are you a member of the Society of</p> <p>16 Gynecologic Oncologists?</p> <p>17 A I am.</p> <p>18 Q You are here as an expert witness for</p> <p>19 defendant Johnson & Johnson in connection with the</p> <p>20 talcum powder product litigation; true?</p> <p>21 A I am.</p> <p>22 Q And you have given four prior depositions</p> <p>23 regarding defendant Johnson & Johnson's talcum</p> <p>24 powder products and the risk of ovarian cancer;</p> <p>25 correct?</p>	<p style="text-align: right;">Page 17</p> <p>1 Q Have you testified in deposition or trial</p> <p>2 in any other talcum powder product cases?</p> <p>3 A No.</p> <p>4 Q You last gave a deposition in the</p> <p>5 Flannigan matter in 2019?</p> <p>6 A I believe that deposition, yes, was in</p> <p>7 2019, that's correct.</p> <p>8 Q Have you given any deposition since then?</p> <p>9 A No.</p> <p>10 Q Is it true that the Flannigan matter did</p> <p>11 not concern talcum powder products or ovarian</p> <p>12 cancer?</p> <p>13 A That's correct.</p> <p>14 Q Did the Flannigan matter concern any of</p> <p>15 the issues as you deem them in this case?</p> <p>16 A No.</p> <p>17 Q The case was totally unrelated to any</p> <p>18 issue in this case; is that true?</p> <p>19 A That's correct.</p> <p>20 MS. CURRY: Object to form.</p> <p>21 THE WITNESS: That's correct.</p> <p>22 BY MS. GARBER:</p> <p>23 Q I know you've just recently given a</p> <p>24 deposition, but I'll just basically re-cover some --</p> <p>25 A I'm sorry, ma'am. May I stop -- I'm</p>

<p style="text-align: right;">Page 18</p> <p>1 sorry.</p> <p>2 Q Of course.</p> <p>3 A In the broadest sense that the Flannigan</p> <p>4 matter did involve causation, then I would say there</p> <p>5 is a similarity between these cases from the</p> <p>6 Flannigan matter. But it wasn't the same type of</p> <p>7 cancer and it wasn't a talcum powder litigation.</p> <p>8 Q What was the nature of the allegations in</p> <p>9 the Flannigan matter?</p> <p>10 A The nature of the allegations was that</p> <p>11 the failure on the part of a practitioner, a medical</p> <p>12 doctor to obtain a Pap smear on a patient led to a</p> <p>13 delay in diagnosis.</p> <p>14 Q Who were you the expert witness for, the</p> <p>15 defense or the plaintiff?</p> <p>16 A The defense.</p> <p>17 Q And it was your opinion that there was no</p> <p>18 delay in diagnosis?</p> <p>19 A It was my opinion that the absence of a</p> <p>20 Pap smear being obtained at the time that plaintiff</p> <p>21 asserted it should have been did not lead to a</p> <p>22 change in the patient's outcome.</p> <p>23 Q In that matter, did you testify about the</p> <p>24 risk factors that may or may not be applicable for</p> <p>25 endomet -- I'm sorry, uterine cancer?</p>	<p style="text-align: right;">Page 20</p> <p>1 BY MS. GARBER:</p> <p>2 Q You understand that you've taken an oath</p> <p>3 to tell the truth under penalty of perjury, which</p> <p>4 carries the same force and effect as if we were</p> <p>5 sitting in a court of law rather than in the</p> <p>6 informal setting of this conference room.</p> <p>7 You understand that, don't you?</p> <p>8 A Yes.</p> <p>9 Q You understand that if you don't</p> <p>10 understand any of my questions, that it's perfectly</p> <p>11 fine for you to ask for clarification; right?</p> <p>12 A Correct.</p> <p>13 Q And I'm going to hope that you will do</p> <p>14 so. If you don't understand the nature of my</p> <p>15 question and you answer it, then I'll assume you</p> <p>16 understood the nature of my question.</p> <p>17 Is that fair?</p> <p>18 A Fair.</p> <p>19 Q You're doing a very good job of not</p> <p>20 talking over the top of me and I'll try to do a good</p> <p>21 job of not doing that. So let's try to avoid that,</p> <p>22 especially as it gets later in the day so we have a</p> <p>23 clear record; okay?</p> <p>24 A Okay.</p> <p>25 Q It's important to be truthful in a</p>
<p style="text-align: right;">Page 19</p> <p>1 A It wasn't a case of uterine cancer, so</p> <p>2 no.</p> <p>3 Q Was it a case of cervical cancer?</p> <p>4 A Yes.</p> <p>5 Q Did you testify about the risk factors</p> <p>6 for that disease?</p> <p>7 A Only in the most general sense. It was</p> <p>8 not really the focus of my testimony.</p> <p>9 Q Was the focus of your testimony relating</p> <p>10 to causation in any way as concerning the risk</p> <p>11 factors for cervical cancer?</p> <p>12 MS. CURRY: Object to form.</p> <p>13 THE WITNESS: Again, not other than in</p> <p>14 the most general sense. My testimony really was</p> <p>15 more about whether or not a Pap smear should have</p> <p>16 been performed at the time the plaintiff asserted it</p> <p>17 should have been.</p> <p>18 MS. GARBER: Thank you.</p> <p>19 BY MS. GARBER:</p> <p>20 Q Let's go over some of the ground rules</p> <p>21 that govern the deposition process just as a review.</p> <p>22 You're sufficiently familiar with ground rules that</p> <p>23 cover the deposition process?</p> <p>24 A I believe I am.</p> <p>25 MS. CURRY: Object to the form.</p>	<p style="text-align: right;">Page 21</p> <p>1 deposition; right?</p> <p>2 A I would agree with that.</p> <p>3 Q Do you agree it's important to be candid</p> <p>4 and fair because this testimony will be, could be</p> <p>5 read and heard by a court and jury?</p> <p>6 MS. CURRY: Objection to the form.</p> <p>7 THE WITNESS: I don't really know what</p> <p>8 will happen with this testimony today, but I agree</p> <p>9 that it's important to be candid and fair.</p> <p>10 BY MS. GARBER:</p> <p>11 Q Do you also agree it's important to tell</p> <p>12 the truth, the whole truth, and not half truths?</p> <p>13 A Absolutely.</p> <p>14 Q We'll go through some of your sort of</p> <p>15 background. Can we agree that it is important for</p> <p>16 you to avoid giving the impression that you are an</p> <p>17 expert in a given area where you have no expertise?</p> <p>18 MS. CURRY: Object to form.</p> <p>19 THE WITNESS: I think I would have to</p> <p>20 have you define what is expertise, because your</p> <p>21 understanding of expertise may not be in agreement</p> <p>22 with my understanding of expertise.</p> <p>23 BY MS. GARBER:</p> <p>24 Q Certainly. But if you understand the</p> <p>25 nature of my question, you won't try to answer</p>

<p style="text-align: right;">Page 22</p> <p>1 questions out of your understood expertise.</p> <p>2 Is that a fair statement?</p> <p>3 A I think that's fair.</p> <p>4 Q For example, you've never conducted</p> <p>5 research regarding the effects of talcum powder</p> <p>6 products including its carcinogenicity; right?</p> <p>7 MS. CURRY: Object to the form.</p> <p>8 THE WITNESS: What do you mean by</p> <p>9 research?</p> <p>10 BY MS. GARBER:</p> <p>11 Q Have you done any research with regard to</p> <p>12 talcum powder products? You yourself, have you done</p> <p>13 any research studies?</p> <p>14 A I'm certainly researched the literature.</p> <p>15 Q But have you done any -- okay, that's</p> <p>16 fair. Have you done any experimentation with regard</p> <p>17 to talcum powder products and ovarian cancer?</p> <p>18 A You mean benchtop research or clinical</p> <p>19 trials research?</p> <p>20 Q Yes?</p> <p>21 A No, I've not done either of those.</p> <p>22 Q With regard to the literature, have</p> <p>23 you -- you yourself, conducted any epidemiological</p> <p>24 studies in connection with talcum powder products</p> <p>25 and ovarian cancer risk?</p>	<p style="text-align: right;">Page 24</p> <p>1 A That's true.</p> <p>2 Q Have you been asked to publish your</p> <p>3 research?</p> <p>4 A I'm sorry. No, I have not.</p> <p>5 Q Have you endeavored to attempt to publish</p> <p>6 your expert report which was issued in connection</p> <p>7 with this litigation, which is dated February 25th,</p> <p>8 2019?</p> <p>9 A No, I have not.</p> <p>10 Q Have you endeavored to publish any of</p> <p>11 your expert reports that you have issued in</p> <p>12 connection with talcum powder product litigation?</p> <p>13 A Well, there's only one other report that</p> <p>14 I've actually ever generated and no, I've not</p> <p>15 endeavored to publish that either.</p> <p>16 Q And that report was the Echeverria</p> <p>17 report; correct?</p> <p>18 A That's correct.</p> <p>19 Q Are you an expert with regard to causes</p> <p>20 of ovarian cancer?</p> <p>21 A So I believe I'm an expert with risk fact</p> <p>22 to risk factors associated with the development of</p> <p>23 ovarian cancer, but I don't believe that we know in</p> <p>24 any one particular patient what causes ovarian</p> <p>25 cancer. I would not use that term.</p>
<p style="text-align: right;">Page 23</p> <p>1 A Do you mean have I published on that?</p> <p>2 Q Yeah.</p> <p>3 A I've not published on that, but I've</p> <p>4 certainly conducted research with the literature in</p> <p>5 the sense of reading it in order to understand it</p> <p>6 and to express an opinion.</p> <p>7 Q And that is the extent of your research</p> <p>8 experience with regard to talcum powder products and</p> <p>9 risk of ovarian cancer; correct?</p> <p>10 MS. CURRY: Object to the form.</p> <p>11 THE WITNESS: So I'm not entirely</p> <p>12 comfortable with what I think is your vague use of</p> <p>13 the term research, because research really does</p> <p>14 encompass many things and what I do on a daily</p> <p>15 basis.</p> <p>16 So if we're discussing benchtop research</p> <p>17 or publishing specifically on the issue of talc and</p> <p>18 ovarian cancer, I've not done either of those. But</p> <p>19 my research experience, I think, is a broader</p> <p>20 definition than perhaps what you're using.</p> <p>21 BY MS. GARBER:</p> <p>22 Q So in connection with the, as you say,</p> <p>23 research that you've done regarding the talcum</p> <p>24 powder products literature, you -- is it true that</p> <p>25 you have not endeavored to publish that research?</p>	<p style="text-align: right;">Page 25</p> <p>1 Q Doctor, haven't you testified a little</p> <p>2 broader than that in the past that you have no idea</p> <p>3 what causes ovarian cancer, not limiting it down to</p> <p>4 a specific patient?</p> <p>5 MS. CURRY: Object to the form.</p> <p>6 THE WITNESS: No, I don't actually think</p> <p>7 that's what my testimony was. I think my testimony</p> <p>8 is that, in terms of what actually causes ovarian</p> <p>9 cancer from a molecular biology standpoint, and with</p> <p>10 respect to any one particular patient, we don't know</p> <p>11 what causes ovarian cancer.</p> <p>12 We certainly know of risk factors that</p> <p>13 are associated with the disease, but in any one</p> <p>14 particular patient, we can't say this is the cause.</p> <p>15 BY MS. GARBER:</p> <p>16 Q Doctor, do you recall when I took your</p> <p>17 deposition in the Echeverria matter on May 9th,</p> <p>18 2017?</p> <p>19 A Yes, I do recall.</p> <p>20 Q And do you recall I was asking you about</p> <p>21 causes of ovarian cancer? Do you recall that?</p> <p>22 A In the general sense; yes.</p> <p>23 Q And, Doctor, I asked you, "So you can't</p> <p>24 think of anything that you could say would cause a</p> <p>25 woman's ovarian cancer?" And Doctor, you answered,</p>

<p style="text-align: right;">Page 26</p> <p>1 quote "I have no idea what causes ovarian cancer." 2 Do you dispute that testimony as you sit 3 here today? 4 MS. SHARKO: Could you just show her the 5 transcript, please? 6 MS. GARBER: I don't have a copy of it. 7 MS. CURRY: May we see your copy that you 8 were just reading from? 9 MS. GARBER: Sure. It's 5 through 17. 10 MS. CURRY: Thank you. 11 THE WITNESS: Right. So this is 12 referring to a woman's cancer, and as I just 13 testified, I don't believe that we have any idea 14 what causes a woman's cancer. The question was in a 15 specific woman and that's how I responded to you. 16 BY MS. GARBER: 17 Q Doctor, nowhere here does it say "in a 18 specific patient." The question was not, in a 19 specific patient do we ever know what causes a 20 woman's ovarian cancer. It was stated, in this most 21 broad sense, so you can't think of anything that you 22 could say would cause a woman's ovarian cancer. And 23 your answer was: I have no idea what causes ovarian 24 cancer? 25 MS. CURRY: Object to form.</p>	<p style="text-align: right;">Page 28</p> <p>1 20 percent. 2 BY MS. GARBER: 3 Q So the majority of the patients that you 4 treat have not been diagnosed with ovarian cancer -- 5 or sorry, with any form of female reproductive 6 cancer? 7 MS. CURRY: Object to the form. 8 THE WITNESS: No. 9 MS. CURRY: Misstates the testimony. 10 THE WITNESS: I think you're completely 11 misstating what I just said. You asked me -- 12 MS. GARBER: I might have misspoke. 13 BY MS. GARBER: 14 Q The majority of your patients have been 15 diagnosed with some form of female reproductive 16 cancer; is that true? 17 A With either invasive cancer or 18 pre-cancer; yes, that's correct. 19 Q How much money have you made to date from 20 defendant Johnson & Johnson testifying about their 21 talcum powder products? 22 MS. CURRY: Object to the form. 23 THE WITNESS: Prior to this MDL 24 litigation? 25 MS. GARBER: Ever.</p>
<p style="text-align: right;">Page 27</p> <p>1 THE WITNESS: No, ma'am, I disagree with 2 you. The question is "a woman." I'm answering your 3 question, which was "a woman." 4 BY MS. GARBER: 5 Q I wasn't asking you about a specific 6 woman. I was asking you about women in general, but 7 that's fine, I'll move on. 8 A But, ma'am, I disagree with you. You 9 actually said "a woman" in your question, so that is 10 an individual patient. And so I was answering you 11 for an individual patient. 12 The question was not women in general. 13 The question was a woman. 14 Q The record stands. 15 How many -- how many papers have you 16 published about the causes of ovarian cancer in the 17 last 19 years? 18 A None. 19 Q What percentage of your current patients 20 have not been diagnosed with female reproductive 21 cancer? 22 MS. CURRY: Object to the form. 23 THE WITNESS: Of any type of cancer? 24 MS. GARBER: Yes. 25 THE WITNESS: I would say maybe</p>	<p style="text-align: right;">Page 29</p> <p>1 THE WITNESS: Ever. So I have not 2 received payment for my last invoice, so to date, I 3 believe I've made around \$390,000. 4 BY MS. GARBER: 5 Q The invoice that you submitted as part of 6 my request for documents, was for 100,000 -- roughly 7 100,500; correct? 8 MS. CURRY: Object to the form. 9 THE WITNESS: It's exactly 100,500. 10 BY MS. GARBER: 11 Q That's for 134 hours of work? 12 A That's correct. 13 Q And that was spanning from December 14 of 2018 to February 2019? 15 A That's correct. 16 Q So if we add that to the previous amount 17 that you've made, that would total roughly -- well, 18 nearly half a million dollars? 19 A Nearly, it would be about \$490,000 over 20 about three and a half years that I've been working 21 in this matter, that's correct. 22 Q And since February of 2019 to today, how 23 many hours have you worked on this case? 24 A I would say maybe 15. 25 Q Have you invoiced for that time yet?</p>

<p style="text-align: right;">Page 30</p> <p>1 A No, I have not.</p> <p>2 Q So the -- we would know that the totality</p> <p>3 of the money that you've generated in connection</p> <p>4 with Johnson & Johnson talcum powder products</p> <p>5 through today by taking roughly 490,000 and adding</p> <p>6 an additional 15 hours of pay at \$750 an hour;</p> <p>7 correct?</p> <p>8 A Over the three years, that's correct.</p> <p>9 Q Have you made other money from</p> <p>10 pharmaceutical companies?</p> <p>11 MS. CURRY: Object to the form.</p> <p>12 THE WITNESS: So I have given talks on</p> <p>13 behalf of Merck and in the past Genentech, speaking</p> <p>14 on behalf of Gardasil, the HPV vaccine.</p> <p>15 Previously I spoke about Avastin, which</p> <p>16 is a drug that we use to treat ovarian and cervical</p> <p>17 cancer.</p> <p>18 BY MS. GARBER:</p> <p>19 Q How much money were you paid from</p> <p>20 pharmaceutical companies aside from Johnson &</p> <p>21 Johnson in 2018?</p> <p>22 A In 2018, I think the number was somewhere</p> <p>23 around maybe \$30,000.</p> <p>24 Q I think you were asked this in a previous</p> <p>25 deposition or testimony that I read, but you are</p>	<p style="text-align: right;">Page 32</p> <p>1 choice of drugs for their patients.</p> <p>2 BY MS. GARBER:</p> <p>3 Q Is it limited to drugs?</p> <p>4 A It is in -- in terms of payments? No, I</p> <p>5 think that even if you go and you have a meal or</p> <p>6 something, then the company reports that as the cost</p> <p>7 associated with you attending a meeting.</p> <p>8 Q So the purpose is to inform patients of</p> <p>9 any undue influence between the physician by</p> <p>10 industry that may affect your medical care and</p> <p>11 treatment of that patient; correct?</p> <p>12 MS. CURRY: Object to the form.</p> <p>13 THE WITNESS: No, I don't believe that's</p> <p>14 what I said. It's the potential. There have been</p> <p>15 some studies that have shown that if physicians are</p> <p>16 reimbursed for issuing certain drugs or certain</p> <p>17 perhaps medications for patients and they're</p> <p>18 collecting money from those companies, that it may</p> <p>19 influence their choices. But it's a potential; it's</p> <p>20 not necessarily a given, as you just stated.</p> <p>21 BY MS. GARBER:</p> <p>22 Q There is potential for undue influence on</p> <p>23 patient care; correct?</p> <p>24 MS. CURRY: Object to the form.</p> <p>25 THE WITNESS: There's potential for undue</p>
<p style="text-align: right;">Page 31</p> <p>1 familiar with the Physician Payments Sunshine Act</p> <p>2 that was passed in 2010?</p> <p>3 A Yes.</p> <p>4 Q What is your understanding of that Act?</p> <p>5 MS. CURRY: Object to form.</p> <p>6 THE WITNESS: With what context?</p> <p>7 BY MS. GARBER:</p> <p>8 Q What did the Act state or what's your</p> <p>9 understanding of it?</p> <p>10 MS. CURRY: Object to the form.</p> <p>11 THE WITNESS: My understanding of it is</p> <p>12 that when I go out and speak, as I do and as I</p> <p>13 stated on behalf of products such as Gardasil or</p> <p>14 Avastin, that the federal government is notified of</p> <p>15 those payments and those are posted for public view</p> <p>16 in the public domain.</p> <p>17 BY MS. GARBER:</p> <p>18 Q What is the reason, as you understand it,</p> <p>19 for the Physician Payments Sunshine Act?</p> <p>20 MS. CURRY: Object to the form.</p> <p>21 THE WITNESS: My understanding is that</p> <p>22 the rationale is that patients have an opportunity</p> <p>23 to go to that site to see if their physicians have</p> <p>24 been collecting monies from those companies because</p> <p>25 that may have undue influence on the physicians'</p>	<p style="text-align: right;">Page 33</p> <p>1 influence on the choices of medications that</p> <p>2 physicians may prescribe.</p> <p>3 BY MS. GARBER:</p> <p>4 Q It's limited only to undue influence on</p> <p>5 prescriptions that physicians may give, it's not</p> <p>6 limited, it's not concerned for undue influence on</p> <p>7 medical care in general, Dr. Saenz?</p> <p>8 MS. CURRY: Object to the form.</p> <p>9 THE WITNESS: So my understanding of the</p> <p>10 published peer-reviewed literature on this topic is</p> <p>11 that it's limited to physicians making choices about</p> <p>12 prescription medications.</p> <p>13 BY MS. GARBER:</p> <p>14 Q Okay. Tell me about your understanding</p> <p>15 of the reporting attendant to the physician's</p> <p>16 payment under the act. Who does the reporting, the</p> <p>17 physician or the industry manufacturer?</p> <p>18 MS. CURRY: Object to the form.</p> <p>19 THE WITNESS: I don't really know the</p> <p>20 nuances of that. I do know that if I receive a</p> <p>21 payment from a company, that that is reported on</p> <p>22 that website. But there are inaccuracies in that</p> <p>23 reporting. There are methods for physicians to</p> <p>24 query into if they feel that the reporting has been</p> <p>25 in error.</p>

<p style="text-align: right;">Page 34</p> <p>1 So I can't honestly tell you how the</p> <p>2 reporting happens. I just know that I don't do the</p> <p>3 reporting. I believe it's the pharmaceutical</p> <p>4 company, but I don't really know. I have no</p> <p>5 personal knowledge of how that happens.</p> <p>6 BY MS. GARBER:</p> <p>7 Q Do you know if Johnson & Johnson</p> <p>8 disclosed the money that they paid you attendant to</p> <p>9 your expert work in this case?</p> <p>10 MS. CURRY: Object to the form.</p> <p>11 THE WITNESS: I don't know.</p> <p>12 BY MS. GARBER:</p> <p>13 Q Did you go and look on the website to see</p> <p>14 if that's disclosed?</p> <p>15 A No, I have not.</p> <p>16 Q You said that you know that you've made</p> <p>17 about 30,000 in 2018. Did you see that that</p> <p>18 included any payments from Johnson & Johnson?</p> <p>19 MS. CURRY: Object to the form.</p> <p>20 THE WITNESS: No.</p> <p>21 MS. CURRY: Misstates the testimony.</p> <p>22 THE WITNESS: I believe I told you that</p> <p>23 was payments from Genentech and Merck specifically.</p> <p>24 So I have not been on the website. I have no idea</p> <p>25 what's reported for me on the website.</p>	<p style="text-align: right;">Page 36</p> <p>1 Q Do you see under the term "general" that</p> <p>2 it indicates payments that are not associated with</p> <p>3 any research study?</p> <p>4 A Yes.</p> <p>5 Q So that is the type -- that is a type of</p> <p>6 payment; correct?</p> <p>7 MS. CURRY: Object to the form.</p> <p>8 THE WITNESS: That's what it says on the</p> <p>9 piece of paper.</p> <p>10 BY MS. GARBER:</p> <p>11 Q If we turn to the second page in, it</p> <p>12 indicates your name; correct?</p> <p>13 A Yes.</p> <p>14 Q Does that indicate your business address,</p> <p>15 3855 Health Sciences Drive?</p> <p>16 A Yes.</p> <p>17 Q That's your work address; correct?</p> <p>18 A That's one of my work addresses.</p> <p>19 Q This is for -- what's your other work</p> <p>20 address?</p> <p>21 A 9300 Campus Point Drive, 200 West Arbor</p> <p>22 Drive. There's -- UCSD has many facilities.</p> <p>23 Q Is this your primary office?</p> <p>24 A This is where my academic office is, yes.</p> <p>25 Q In connection with University of</p>
<p style="text-align: right;">Page 35</p> <p>1 BY MS. GARBER:</p> <p>2 Q You did work for Johnson & Johnson in</p> <p>3 2017; correct?</p> <p>4 A Yes.</p> <p>5 Q Did you look at the website to see what</p> <p>6 the disclosure was of your payments in 2017?</p> <p>7 A No.</p> <p>8 MS. CURRY: Object to the form.</p> <p>9 THE WITNESS: I've not been on the</p> <p>10 website.</p> <p>11 BY MS. GARBER:</p> <p>12 Q Okay.</p> <p>13 (C. Saenz Exhibit 1 was marked for</p> <p>14 identification.)</p> <p>15 BY MS. GARBER:</p> <p>16 Q As Exhibit 1, Doctor, I will represent to</p> <p>17 you that the -- this document I obtained from the</p> <p>18 Openpaymentsdata.cms.gov website for the physician</p> <p>19 profile of Cheryl Saenz.</p> <p>20 Do you see that by turning to page two of</p> <p>21 this document?</p> <p>22 A Okay.</p> <p>23 Q Doctor, on the first page, I printed out</p> <p>24 the payment type definitions. Do you see that?</p> <p>25 A Yes.</p>	<p style="text-align: right;">Page 37</p> <p>1 California San Diego; correct?</p> <p>2 A Correct.</p> <p>3 Q So it looks like this is a disclosure of</p> <p>4 a payment from the year 2013; correct?</p> <p>5 MS. CURRY: Objection to the form.</p> <p>6 THE WITNESS: It's a listing of a general</p> <p>7 payment in the year 2013, correct.</p> <p>8 BY MS. GARBER:</p> <p>9 Q All right. If you go under about midway</p> <p>10 through the page, it says "general payments";</p> <p>11 correct?</p> <p>12 A (No audible response.)</p> <p>13 Q Right above the amount?</p> <p>14 A Yes.</p> <p>15 Q It indicates that you received general</p> <p>16 payments in the amount of 3,151.88; correct?</p> <p>17 A Correct.</p> <p>18 Q That was listed above the national mean</p> <p>19 by about \$1,500; correct?</p> <p>20 A Correct.</p> <p>21 Q If we turn to what is listed at the</p> <p>22 bottom, page one of three, it gives us the</p> <p>23 manufacturer who made that payment here: Merck,</p> <p>24 Sharp & Dohme; correct?</p> <p>25 MS. CURRY: I'm sorry.</p>

<p style="text-align: right;">Page 38</p> <p>1 THE WITNESS: I don't have page numbers. 2 BY MS. GARBER: 3 Q If you look at the right-hand corner? 4 A There's no page numbers. 5 Q Can you go one page in. 6 A There's no page numbers. 7 Q All right. If you turn four pages in, do 8 you see that the manufacturer was Merck, Sharp, & 9 Dohme who made that payment of 3,100? 10 A Are you referring to this bar graph? 11 Q Yes. 12 A At the bottom? 13 Q Yes. 14 A Yes. 15 Q Then if you go a couple pages further, we 16 come to the payments you received in 2014. Do you 17 see that? 18 A Yes. 19 Q There you received general payments in 20 the amount of \$25,751.41; is that correct? 21 A Correct. 22 Q And there this is above the national mean 23 for physicians by amount of 22,000-some dollars; 24 correct? 25 A Correct.</p>	<p style="text-align: right;">Page 40</p> <p>1 A But you asked me for my explanation -- 2 MS. CURRY: I'm sorry. 3 THE WITNESS: -- of what these payments 4 are -- 5 BY MS. GARBER: 6 Q Do you understand that we're here, I'm 7 asking you questions and you're answering them, 8 Doctor? 9 A I'm trying -- 10 MS. CURRY: She tried to clarify. 11 MS. GARBER: You answered my question and 12 there was no question pending, but go ahead. 13 THE WITNESS: I want to clarify 14 completely, because you had me skip past several 15 pages that actually talk about what some of these 16 payments are for. And some of these payments are 17 for travel expenses to the venue. Some of these 18 payments are for food and beverage that was consumed 19 at these. 20 So they're not all just payments. I just 21 want to make sure we're clarifying exactly what 22 these monies are. They're not all just payments. 23 BY MS. GARBER: 24 Q Okay, Doctor. The total that you were 25 paid by these medical manufacturers in the year of</p>
<p style="text-align: right;">Page 39</p> <p>1 Q The bar, so we understand the nature of 2 this document, the bar graph at the bottom is 3 showing the national average for physicians, and 4 then the sliding scale there with the person showing 5 what you made, \$25,000, which is off to the right 6 above the national average, is that a fair 7 understanding of what that means? 8 A That's what the picture shows. 9 MS. CURRY: Object to the form. 10 THE WITNESS: I don't necessarily know 11 what the intent of that is, but that's what the 12 picture shows. 13 BY MS. GARBER: 14 Q Okay. And going a couple of pages back, 15 we see for 2014 that you were paid by the industry 16 manufacturers Genentech and Merck, Sharp & Dohme; 17 correct? 18 A Correct. 19 Q If we go a couple more pages forward, we 20 come to the year 2015. Are we there? 21 A Yes. 22 Q In 2015, you made \$47,095.28; correct? 23 A According to this. But I want to qualify 24 something here. 25 Q Doctor, I didn't have a question pending.</p>	<p style="text-align: right;">Page 41</p> <p>1 2015 was \$47,095.28; true or false? 2 MS. CURRY: Object to the form. 3 THE WITNESS: So the total payments I 4 received include reimbursements as well as payments 5 for giving a talk. So I think it's important to be 6 complete in what we're looking at. 7 MS. GARBER: Fair enough. 8 BY MS. GARBER: 9 Q And, Doctor, if you turn a few pages more 10 we come to 2016. Are you there? 11 A No. Okay. 12 Q There you were paid \$15,606.79, which is 13 above -- again above the national mean by 14 physicians; correct? 15 A That's what the picture shows; yes. 16 Q We go a couple pages back, we see that 17 the medical manufacturers that paid you in 2016 were 18 again Genentech and Merck Sharp; is that true? 19 A Couple pages back or a couple pages 20 forward? 21 Q I'm sorry, forward. 22 A Yes, that's correct. 23 Q Now let's get to 2017. This document 24 reflects that in 2017, you were paid \$31,060.06; 25 correct?</p>

<p style="text-align: right;">Page 42</p> <p>1 A I received payments in that amount;</p> <p>2 correct.</p> <p>3 Q If we go a couple pages forward, we see</p> <p>4 the listing of the same medical manufacturers,</p> <p>5 Genentech and Merck Sharp, who made that payment;</p> <p>6 correct?</p> <p>7 A Correct.</p> <p>8 Q Doctor, does this reflect the money that</p> <p>9 you made from Johnson & Johnson in 2017?</p> <p>10 A It doesn't appear to.</p> <p>11 MS. CURRY: Object to the form.</p> <p>12 BY MS. GARBER:</p> <p>13 Q Does it reflect the roughly 300 and some</p> <p>14 thousand dollars that you earned with regard to</p> <p>15 talcum powder products from Johnson & Johnson?</p> <p>16 MS. CURRY: Object to the form.</p> <p>17 THE WITNESS: Well, in 2017, I didn't</p> <p>18 make 300,000 and something, but in 2017 in this</p> <p>19 particular document that you've handed me, there</p> <p>20 doesn't seem to be any notation about the monies</p> <p>21 that I did make from Johnson & Johnson.</p> <p>22 BY MS. GARBER:</p> <p>23 Q How much money did you make from Johnson</p> <p>24 & Johnson in 2017?</p> <p>25 A I don't actually know the breakdown.</p>	<p style="text-align: right;">Page 44</p> <p>1 that I earned about \$30,000 in income from Merck and</p> <p>2 Genentech. But I've actually never looked at this</p> <p>3 website, never seen any of these documents until you</p> <p>4 showed me this today.</p> <p>5 BY MS. GARBER:</p> <p>6 Q Okay. I'm not showing you documents from</p> <p>7 2018 because they're not on the website. Okay?</p> <p>8 A Good to know.</p> <p>9 Q All right. Do physicians receiving</p> <p>10 substantial sums of money from the medical industry</p> <p>11 have an obligation to disclose those transactions --</p> <p>12 MS. CURRY: Object --</p> <p>13 MS. GARBER: -- to their patients?</p> <p>14 MS. CURRY: Object to the form.</p> <p>15 THE WITNESS: With respect to what</p> <p>16 exactly?</p> <p>17 BY MS. GARBER:</p> <p>18 Q Do they have an obligation to disclose to</p> <p>19 their patients that they have been paid by medical</p> <p>20 manufacturers in general, we'll start there?</p> <p>21 MS. CURRY: Object to the form.</p> <p>22 THE WITNESS: So in general, I don't</p> <p>23 think there is a general obligation to make such a</p> <p>24 disclosure unless the particular product or</p> <p>25 medication that you were discussing with a patient</p>
<p style="text-align: right;">Page 43</p> <p>1 Q What's your best estimate?</p> <p>2 MS. CURRY: Object to the form.</p> <p>3 THE WITNESS: I'd be guessing.</p> <p>4 BY MS. GARBER:</p> <p>5 Q We don't want you to guess, but your best</p> <p>6 estimate?</p> <p>7 A I'd be guessing. I only know --</p> <p>8 Q Is it more than 100,000?</p> <p>9 MS. CURRY: Object to the form.</p> <p>10 THE WITNESS: I think it might be</p> <p>11 slightly more than 100,000.</p> <p>12 BY MS. GARBER:</p> <p>13 Q Thanks. So as I went through this group</p> <p>14 of documents, it looks like it adds up to over</p> <p>15 \$100,000 spanning from 2013 to 2017; correct?</p> <p>16 A Well, it's through 2017, so that's five</p> <p>17 years, yes.</p> <p>18 Q Then you told me that you thought you had</p> <p>19 looked at 2018 CMCS and had seen that you had made</p> <p>20 another \$30,000?</p> <p>21 MS. CURRY: Object to the form, misstates</p> <p>22 the testimony.</p> <p>23 THE WITNESS: So that's not what I said</p> <p>24 at all. I specifically told you that I've not</p> <p>25 looked at the website, but that my recollection is</p>	<p style="text-align: right;">Page 45</p> <p>1 is from a company that you have received monies</p> <p>2 from.</p> <p>3 So for example, if I'm discussing with a</p> <p>4 patient whether or not she should get the Gardasil</p> <p>5 vaccine, I actually do tell patients that I speak on</p> <p>6 behalf of the Gardasil vaccine and that I am paid</p> <p>7 for such talks.</p> <p>8 BY MS. GARBER:</p> <p>9 Q What is the reason that you should do</p> <p>10 that?</p> <p>11 A So that there's transparency. So that</p> <p>12 patients know that you may actually have information</p> <p>13 that could potentially bias you towards making such</p> <p>14 a recommendation. But I think that patients knowing</p> <p>15 that are able to make an informed consent as to</p> <p>16 whether or not they want to go ahead and pursue</p> <p>17 whatever is your recommendation.</p> <p>18 Q Do you tell each and every patient that</p> <p>19 you care for your work that you're doing for Johnson</p> <p>20 & Johnson in connection with this litigation?</p> <p>21 A So I don't tell each and every patient</p> <p>22 because I don't think it's influential in each and</p> <p>23 every patient. I only tell patients if specifically</p> <p>24 they ask me questions about talc.</p> <p>25 Q Have you ever written a paper on this</p>

<p style="text-align: right;">Page 46</p> <p>1 topic, Doctor?</p> <p>2 MS. CURRY: Object to the form.</p> <p>3 THE WITNESS: What topic are we</p> <p>4 discussing now?</p> <p>5 BY MS. GARBER:</p> <p>6 Q Disclosing payments from medical</p> <p>7 manufacturers and the importance of that?</p> <p>8 A No, I have not.</p> <p>9 (C. Saenz Exhibit 2 was marked for</p> <p>10 identification.)</p> <p>11 BY MS. GARBER:</p> <p>12 Q I'll mark as Exhibit 2 a paper. It</p> <p>13 indicates original research and it's titled</p> <p>14 "Industry Payments to Obstetrician Gynecologists and</p> <p>15 Analysis of 2014 Open Payments Data."</p> <p>16 Did I read that title correctly?</p> <p>17 A Yes.</p> <p>18 Q Are you listed as an author?</p> <p>19 A As a coauthor; yes.</p> <p>20 Q So do you now believe that you have</p> <p>21 published in this area?</p> <p>22 A I don't believe this is about disclosure.</p> <p>23 This is about the payments that are being received.</p> <p>24 So the actual disclosure to patients and</p> <p>25 that as a topic is not actually what the topic of</p>	<p style="text-align: right;">Page 48</p> <p>1 and to centers for Medicare and Medicaid service.</p> <p>2 Did I read that correctly?</p> <p>3 A Yes.</p> <p>4 Q If you turn to page 377, in the left-hand</p> <p>5 column, last -- or near the top, the paragraph that</p> <p>6 begins, "the primary objective."</p> <p>7 Do you see that? It's near the top on</p> <p>8 the left-hand column?</p> <p>9 A Yes.</p> <p>10 Q It indicates as to your secondary</p> <p>11 objective, it was to "promote awareness of published</p> <p>12 payments to encourage OB-GYNs to participate in</p> <p>13 disclosure of their fiscal relationship to patients</p> <p>14 and to make an active role in maintaining accuracy</p> <p>15 of their payment data."</p> <p>16 Did I read that correctly?</p> <p>17 MS. CURRY: To take an active role.</p> <p>18 THE WITNESS: No, you transposed "take"</p> <p>19 to "make."</p> <p>20 BY MS. GARBER:</p> <p>21 Q Okay. To take an active role in</p> <p>22 maintaining accuracy of their payment date?</p> <p>23 A Correct.</p> <p>24 Q Have I read that correctly now?</p> <p>25 A Yes.</p>
<p style="text-align: right;">Page 47</p> <p>1 this paper is.</p> <p>2 Q What is the topic of this paper?</p> <p>3 A The topic of this paper is taking a look</p> <p>4 at what kind of monies physicians are earning from</p> <p>5 industry.</p> <p>6 Q Okay, well, let's go through some of</p> <p>7 this. On the first page, in the right-hand column</p> <p>8 about three quarters of way down, do you see the</p> <p>9 sentence that begins the Physician Payments Sunshine</p> <p>10 Act?</p> <p>11 A Yes.</p> <p>12 Q And that's what we were talking about</p> <p>13 earlier; correct?</p> <p>14 A Correct.</p> <p>15 Q And there it defines the physician</p> <p>16 sunshine Act that was passed in 2014; correct?</p> <p>17 A Correct.</p> <p>18 Q It says --</p> <p>19 A Actually, it's 2010.</p> <p>20 Q I'm sorry, I misspoke. In 2010. It</p> <p>21 indicates that the Physician Payments Sunshine Act</p> <p>22 was passed in 2010 as part of the Affordable Care</p> <p>23 Act and it mandates that medical manufacturers</p> <p>24 report financial relationships in the form of</p> <p>25 payments made to physicians and teaching hospitals,</p>	<p style="text-align: right;">Page 49</p> <p>1 Q If you turn to page 381; okay?</p> <p>2 Under the discussion section, do you see</p> <p>3 is the sentence beginning "according to the</p> <p>4 recommendations"?</p> <p>5 A No.</p> <p>6 Q It's about three quarters of the way</p> <p>7 down?</p> <p>8 A Okay.</p> <p>9 Q It reads, "according to the</p> <p>10 recommendations by the college's ethics committee,</p> <p>11 physicians receiving substantial sums of money from</p> <p>12 the medical industry have a particular obligation to</p> <p>13 their patients to disclose these transactions, and</p> <p>14 to discuss their effects on clinical decision</p> <p>15 making."</p> <p>16 Did I read that correctly?</p> <p>17 A Yes.</p> <p>18 Q That's the obligation under the ethics;</p> <p>19 correct?</p> <p>20 A Right.</p> <p>21 Q If we go over to the right-hand side,</p> <p>22 about halfway down on page 381, do you see the</p> <p>23 sentence which begins "a large part"?</p> <p>24 A Yes.</p> <p>25 Q "A large part of this uncertainty is the</p>

<p style="text-align: right;">Page 50</p> <p>1 result of the complexities involved in defining and</p> <p>2 identifying when clinical integrity is compromised</p> <p>3 by physical relationships with industry."</p> <p>4 Did I read that correctly?</p> <p>5 A No, you did not.</p> <p>6 Q Fiscal. Sorry. I said physical, didn't</p> <p>7 I. Fiscal relationships with industry.</p> <p>8 Did I read that correctly?</p> <p>9 A Yes.</p> <p>10 Q Then it goes on to say, "perhaps the</p> <p>11 final important conclusion to be made from this work</p> <p>12 is that physicians have an opportunity to play</p> <p>13 crucial roles in promoting transparency and managing</p> <p>14 conflicts of interest. By discussing industry</p> <p>15 payments with patients and in maintaining accuracy</p> <p>16 of posted information, doctors can help maximize the</p> <p>17 beneficial effects of disclosure and avoid</p> <p>18 inappropriate influence."</p> <p>19 Did I read that correctly?</p> <p>20 A Yes.</p> <p>21 Q Do you agree with that?</p> <p>22 A Completely.</p> <p>23 Q You wrote that, didn't you?</p> <p>24 A Along with the other authors in this</p> <p>25 paper.</p>	<p style="text-align: right;">Page 52</p> <p>1 those payments are posted.</p> <p>2 A Where are you reading from again?</p> <p>3 Q (No audible response.)</p> <p>4 A Ma'am, where are you reading from?</p> <p>5 Q I'm looking for it. Hold on, please.</p> <p>6 On the right-hand column on 381, it says,</p> <p>7 "by discussing industry payments with patients and</p> <p>8 in maintaining accuracy of the posted information,</p> <p>9 doctors can help maximize the benefits"?</p> <p>10 A Right. And I do discuss payments with my</p> <p>11 patients for anything that comes up that actually</p> <p>12 has to do with the agents involved in the reason</p> <p>13 that I receive those payments.</p> <p>14 Q Doctor, are you making \$1,200 here today</p> <p>15 from Johnson & Johnson in connection with your</p> <p>16 deposition?</p> <p>17 A No.</p> <p>18 Q How much are you making an hour?</p> <p>19 A 1,200 an hour.</p> <p>20 Q Does UCSD know that you're doing expert</p> <p>21 work on behalf of Johnson & Johnson?</p> <p>22 A Yes.</p> <p>23 Q In connection -- I'm sorry. In</p> <p>24 connection with the talcum powder product</p> <p>25 litigation?</p>
<p style="text-align: right;">Page 51</p> <p>1 Q Finally, at the end of this paper, it</p> <p>2 reads, "ongoing involvement from both physicians and</p> <p>3 medical industry will ensure reliable data are made</p> <p>4 available to the public."</p> <p>5 Did I read that correctly?</p> <p>6 A Yes.</p> <p>7 Q So both parties have an obligation, the</p> <p>8 physician and the manufacturer, to be sure that</p> <p>9 there is disclosure of the payments so that patients</p> <p>10 are informed as to whether or not their physician</p> <p>11 has a potential conflict of interest; true?</p> <p>12 MS. CURRY: Object to the form.</p> <p>13 THE WITNESS: Both parties don't have an</p> <p>14 obligation to post information on the website.</p> <p>15 MS. GARBER: I didn't say that, Doctor.</p> <p>16 THE WITNESS: Ma'am, you said both</p> <p>17 parties have an obligation, and the obligation of</p> <p>18 the pharmaceutical company is to post the</p> <p>19 information to the website.</p> <p>20 My obligation is to disclose when I have</p> <p>21 a potential conflict of interest to my patients, and</p> <p>22 I do that.</p> <p>23 BY MS. GARBER:</p> <p>24 Q And, Doctor, in this paper, you wrote,</p> <p>25 that both parties have an obligation to be sure that</p>	<p style="text-align: right;">Page 53</p> <p>1 A Yes, they do.</p> <p>2 Q Are you aware that the United States</p> <p>3 Senate is investigating whether or not Johnson &</p> <p>4 Johnson lied about asbestos being in the products?</p> <p>5 MS. CURRY: Object to the form.</p> <p>6 THE WITNESS: So I'm aware that --</p> <p>7 basically through the nightly news that there's an</p> <p>8 investigation as to whether or not there actually</p> <p>9 was some knowledge as to whether or not asbestos was</p> <p>10 in the baby powder litigation, but other than that,</p> <p>11 other than what's reported on the nightly news, I'm</p> <p>12 not aware of what specific agency is investigating,</p> <p>13 no.</p> <p>14 BY MS. GARBER:</p> <p>15 Q Have you seen any written media coverage.</p> <p>16 You said the nightly news. Have you seen any</p> <p>17 newspaper articles?</p> <p>18 A No.</p> <p>19 MS. SHARKO: Is this the one where your</p> <p>20 expert testified?</p> <p>21 BY MS. GARBER:</p> <p>22 Q Your report in this case indicates that</p> <p>23 you served as chair of the Moores UCSD cancer</p> <p>24 center; is that correct?</p> <p>25 A No.</p>

<p style="text-align: right;">Page 54</p> <p>1 Q You --</p> <p>2 A That's not correct.</p> <p>3 Q I thought I read that -- what is your</p> <p>4 connection with the Moores UCSD cancer center? What</p> <p>5 is your involvement?</p> <p>6 A I'm a faculty physician there.</p> <p>7 Q You haven't been chair of the department?</p> <p>8 A No, and I didn't put that in my report.</p> <p>9 That's inaccurate.</p> <p>10 Q When were you first retained by Johnson &</p> <p>11 Johnson in connection with this litigation? What</p> <p>12 was the very first date as you remember it?</p> <p>13 MS. CURRY: Object to the form. Just to</p> <p>14 clarify for the record, do you mean any talcum</p> <p>15 powder product litigation or the MDL?</p> <p>16 MS. GARBER: No, any talc powder</p> <p>17 litigation.</p> <p>18 THE WITNESS: Any talcum powder</p> <p>19 litigation? November of 2016.</p> <p>20 BY MS. GARBER:</p> <p>21 Q How was it that you were retained in this</p> <p>22 matter?</p> <p>23 MS. CURRY: Object to the form.</p> <p>24 THE WITNESS: I was -- I have a vague</p> <p>25 recollection of receiving a phone call and asking if</p>	<p style="text-align: right;">Page 56</p> <p>1 Lee is a partner with my law firm.</p> <p>2 BY MS. GARBER:</p> <p>3 Q So when you were first retained, you</p> <p>4 indicated that you had already reviewed some</p> <p>5 literature -- you had already been aware of some</p> <p>6 literature with regard to perineal talc and risk of</p> <p>7 ovarian cancer; is that true?</p> <p>8 A Correct.</p> <p>9 Q What literature was that?</p> <p>10 A I don't recall specifically, but it</p> <p>11 wasn't the first time that I had heard about the</p> <p>12 issue of a possible association between the use of</p> <p>13 perineal talc and the development of ovarian cancer.</p> <p>14 Q Were you consequently sent some</p> <p>15 literature?</p> <p>16 MS. CURRY: Object to the form.</p> <p>17 THE WITNESS: I was sent a flash drive</p> <p>18 with some articles on it.</p> <p>19 BY MS. GARBER:</p> <p>20 Q Did you conduct your own research?</p> <p>21 A At what point?</p> <p>22 Q At that point. When you were retained,</p> <p>23 did you conduct your own research for medical</p> <p>24 articles or did you rely on the lawyers to give you</p> <p>25 that literature?</p>
<p style="text-align: right;">Page 55</p> <p>1 I knew of the purported risks of developing ovarian</p> <p>2 cancer associated with the uses of perineal talc and</p> <p>3 whether or not I would be interested in reviewing</p> <p>4 more of the literature than I had already reviewed</p> <p>5 and giving opinions on that particular topic.</p> <p>6 BY MS. GARBER:</p> <p>7 Q Who approached you first?</p> <p>8 A I think I received a phone call from a</p> <p>9 gentleman named Brian Lee.</p> <p>10 Q Did you know Mr. Lee prior to that phone</p> <p>11 call?</p> <p>12 A No.</p> <p>13 Q Did he offer any opinions about perineal</p> <p>14 talc and risk of ovarian cancer?</p> <p>15 MS. CURRY: I'm sorry, I'm going to</p> <p>16 instruct you not to disclose any communications with</p> <p>17 counsel.</p> <p>18 BY MS. GARBER:</p> <p>19 Q Did you understand Mr. Lee to be a</p> <p>20 lawyer?</p> <p>21 A I don't honestly recall that I knew that.</p> <p>22 I knew that he was from a law firm, but I don't know</p> <p>23 if he was a paralegal or a legal. But I knew he was</p> <p>24 in a law firm.</p> <p>25 MS. CURRY: I can stipulate that Brian</p>	<p style="text-align: right;">Page 57</p> <p>1 A Oh. I mean, over the time course of</p> <p>2 researching the issue, I conducted my own research</p> <p>3 as well.</p> <p>4 Q Do you still have that flash drive?</p> <p>5 A I don't think so.</p> <p>6 Q By the way, do you have a file in this</p> <p>7 case?</p> <p>8 MS. CURRY: Object to the form.</p> <p>9 THE WITNESS: What do you mean by a</p> <p>10 "file"?</p> <p>11 BY MS. GARBER:</p> <p>12 Q What's your understanding of the word</p> <p>13 "file"?</p> <p>14 A Like a shadow file?</p> <p>15 Q Do you have any kind of file in</p> <p>16 connection with your work in this case?</p> <p>17 A No. I have my report and I have the</p> <p>18 articles that I've used to read about the issues.</p> <p>19 Q Where are those articles?</p> <p>20 A On my computer.</p> <p>21 Q You don't have any printed articles?</p> <p>22 A No.</p> <p>23 Q Not one?</p> <p>24 A Not one.</p> <p>25 Q In connection with writing your expert</p>

<p style="text-align: right;">Page 58</p> <p>1 report in this case, did you make any notes?</p> <p>2 A So as I was reading plaintiffs' reports</p> <p>3 and depositions, I would make notes on the computer</p> <p>4 for statements of the experts that I would want to</p> <p>5 make comments on in order to incorporate it into my</p> <p>6 report. But it was basically my report outline of</p> <p>7 things that I wanted to incorporate, but that is my</p> <p>8 report.</p> <p>9 Q Did you produce those notes that you made</p> <p>10 when you were reviewing expert reports and the like?</p> <p>11 MS. CURRY: Object to the form.</p> <p>12 THE WITNESS: No, it's the draft of my</p> <p>13 report. So it is my report. So I mean, I have</p> <p>14 produced it, but that's my report.</p> <p>15 BY MS. GARBER:</p> <p>16 Q So when you were making notes about a</p> <p>17 given deposition, you were making a note of that on</p> <p>18 your computer and now it's your testimony that</p> <p>19 became your expert report?</p> <p>20 A Right. I make a note, I'd say for</p> <p>21 example, oh, there's something on page nine of this</p> <p>22 person's thing, and put it in there. And then</p> <p>23 when -- I'd skip some pages, write some more, come</p> <p>24 back to that. So that it was there in the report as</p> <p>25 I was drafting the report.</p>	<p style="text-align: right;">Page 60</p> <p>1 could make sure that I could read it and capture the</p> <p>2 essence of what it was that I was trying to point</p> <p>3 out.</p> <p>4 Sometimes if it was just numbers, I'd</p> <p>5 have the report open, and then I'd have the article</p> <p>6 open at the same time and I'd be reading it as I</p> <p>7 would type my report.</p> <p>8 Q Okay. You understand that Johnson &</p> <p>9 Johnson is the manufacturer of baby powder products</p> <p>10 and formerly Shower to Shower talcum powder product;</p> <p>11 correct?</p> <p>12 A That's my understanding.</p> <p>13 Q You're aware that women use defendant's</p> <p>14 talcum powder products for feminine hygiene?</p> <p>15 MS. CURRY: Object to the form.</p> <p>16 THE WITNESS: I mean, I don't know that I</p> <p>17 would say feminine hygiene. I would say I know that</p> <p>18 they do put on it their perineum or on their bodies,</p> <p>19 on their groins, in different parts. So yes.</p> <p>20 BY MS. GARBER:</p> <p>21 Q What's your understanding of why women</p> <p>22 put talcum powder product on their genitals?</p> <p>23 MS. CURRY: Object to the form.</p> <p>24 THE WITNESS: I think it's variable.</p> <p>25 ///</p>
<p style="text-align: right;">Page 59</p> <p>1 Q Did you write every word of your expert</p> <p>2 report, and when I say "expert report," I'm meaning</p> <p>3 the MDL report dated February 25th, 2019.</p> <p>4 A Did I write every word? Absolutely.</p> <p>5 Q Do you have any drafts or copies or</p> <p>6 notes?</p> <p>7 MS. CURRY: Object to the form.</p> <p>8 THE WITNESS: Of?</p> <p>9 BY MS. GARBER:</p> <p>10 Q Of your report.</p> <p>11 A No. I mean, it was an evolving process</p> <p>12 that just kept getting morphed every time I would</p> <p>13 add to it.</p> <p>14 Q You said you reviewed the literature</p> <p>15 online. Did you make any highlights electronically</p> <p>16 of that literature?</p> <p>17 A No.</p> <p>18 Q Or notes?</p> <p>19 A No.</p> <p>20 Q How was it that you tracked what you</p> <p>21 wanted to recall or remember or note about a given</p> <p>22 piece of literature?</p> <p>23 A So I'd go to the article itself, I'd</p> <p>24 highlight it, and you can snapshot that paragraph or</p> <p>25 whatever and then put it into my report so that I</p>	<p style="text-align: right;">Page 61</p> <p>1 BY MS. GARBER:</p> <p>2 Q What's your understanding of some of the</p> <p>3 reasons?</p> <p>4 A I think some women do it because they</p> <p>5 like the softness. I think some women do it because</p> <p>6 they like the fragrance. I think some women do it</p> <p>7 because they are sweaters and they want to try to</p> <p>8 stay dry. I think there are various uses.</p> <p>9 Q Do you have any first-hand information</p> <p>10 about the manner in which women use it, the manner</p> <p>11 in which they apply it, the amount, the nature of</p> <p>12 how it's applied?</p> <p>13 MS. CURRY: Object to the form.</p> <p>14 THE WITNESS: I don't really know what</p> <p>15 you mean.</p> <p>16 MS. GARBER: Sure.</p> <p>17 BY MS. GARBER:</p> <p>18 Q You don't -- you don't have any firsthand</p> <p>19 information about the way in which women applied it;</p> <p>20 in other words, did they shake it on their hands,</p> <p>21 did they shake it directly on their genitals, did</p> <p>22 they apply it to toilet paper and then apply it.</p> <p>23 In other words, you don't have any of</p> <p>24 these details, do you?</p> <p>25 MS. CURRY: Object to the form.</p>

Page 62	Page 64
<p>1 THE WITNESS: Firsthand?</p> <p>2 MS. GARBER: Yes.</p> <p>3 THE WITNESS: I disagree.</p> <p>4 BY MS. GARBER:</p> <p>5 Q You do?</p> <p>6 A Uh-huh.</p> <p>7 Q What's your firsthand knowledge?</p> <p>8 A I've used it.</p> <p>9 Q Okay. Besides yourself.</p> <p>10 A But that is firsthand knowledge.</p> <p>11 Q All right. You don't have any firsthand</p> <p>12 knowledge of how other women use it, do you?</p> <p>13 MS. CURRY: Object to the form.</p> <p>14 THE WITNESS: I have not personally</p> <p>15 watched another woman apply baby powder to herself,</p> <p>16 that is correct.</p> <p>17 BY MS. GARBER:</p> <p>18 Q And the literature, the epidemiological</p> <p>19 literature does not describe the way in which it was</p> <p>20 applied, and in that regard, I mean was it applied</p> <p>21 to the hand, was it applied to tissue, doesn't give</p> <p>22 that kind of detail, how much was applied at any</p> <p>23 given time?</p> <p>24 MS. CURRY: Object to the form.</p> <p>25 THE WITNESS: So I've not read anything</p>	<p>1 published in, say, 2000, 2010, knowing that on</p> <p>2 average women used baby powder for at least 20 years</p> <p>3 when they were users, that if somebody was diagnosed</p> <p>4 with ovarian cancer in 2000, that most likely she</p> <p>5 would have used it in the 70s or 80s.</p> <p>6 So I do believe that that's the case.</p> <p>7 BY MS. GARBER:</p> <p>8 Q So the point is women were exposed to</p> <p>9 Johnson & Johnson baby powder products in the 50s,</p> <p>10 60s, and 70s and have ovarian cancer; correct?</p> <p>11 MS. CURRY: Object to the form.</p> <p>12 THE WITNESS: I do believe that there</p> <p>13 were some women that probably used it then and then</p> <p>14 had ovarian cancer in later years; yes.</p> <p>15 BY MS. GARBER:</p> <p>16 Q Let's talk about talcum powder product.</p> <p>17 You understand that Johnson & Johnson's baby powder</p> <p>18 and Shower to Shower are talcum powder products;</p> <p>19 correct?</p> <p>20 A I believe that one of the constituents of</p> <p>21 each of those products is talcum powder; correct.</p> <p>22 Q And in your report, when you use the word</p> <p>23 "talc," what do you mean?</p> <p>24 A Baby powder products.</p> <p>25 Q And do you make an assumption that within</p>
Page 63	Page 65
<p>1 that talks about how many shakes, but there are</p> <p>2 certainly studies that talk about women applying it</p> <p>3 to diaphragms or women applying it to their perineum</p> <p>4 or women applying it to their sanitary napkins.</p> <p>5 I do believe that many of the studies</p> <p>6 have looked at and asked those questions. But in</p> <p>7 terms of an in-depth analysis of what constitutes a</p> <p>8 dose per se and how many shakes, no, I'm not aware</p> <p>9 of that.</p> <p>10 BY MS. GARBER:</p> <p>11 Q Are you aware of data that indicates</p> <p>12 there are women -- there are women now with ovarian</p> <p>13 cancer who used talc on their genitals in the 1950s,</p> <p>14 60s, and early 70s?</p> <p>15 MS. CURRY: Object to the form.</p> <p>16 THE WITNESS: Can you say that again?</p> <p>17 BY MS. GARBER:</p> <p>18 Q Sure. Are you aware of data that</p> <p>19 indicates there are women now with ovarian cancer</p> <p>20 that used genital talc in the 1950s, 60s, and early</p> <p>21 70s?</p> <p>22 MS. CURRY: Same objection.</p> <p>23 THE WITNESS: So I'd have to kind of do</p> <p>24 like a retrospective time point. I do believe that</p> <p>25 if we look at some of the studies that were</p>	<p>1 Johnson & Johnson's talcum powder products there is</p> <p>2 no asbestos?</p> <p>3 A I don't believe that what's the</p> <p>4 constituents of the baby powder actually matters to</p> <p>5 my opinion. My opinion is the same regardless,</p> <p>6 because I do believe that if there is a risk of</p> <p>7 developing ovarian cancer with the use of talc,</p> <p>8 regardless of what's in that -- in that product,</p> <p>9 there would be an increased risk of developing</p> <p>10 ovarian cancer, borne out in the literature.</p> <p>11 Q Doctor, my question was a little</p> <p>12 different. Do you make assumptions about the</p> <p>13 constituents of Johnson & Johnson talcum powder</p> <p>14 products when you render your opinions in your</p> <p>15 expert report?</p> <p>16 MS. CURRY: Object to the form.</p> <p>17 THE WITNESS: No, I don't make any</p> <p>18 assumptions.</p> <p>19 BY MS. GARBER:</p> <p>20 Q Is it your opinion that Johnson & Johnson</p> <p>21 baby powder products do not contain talc -- sorry,</p> <p>22 do not contain asbestos?</p> <p>23 A So I'm going to defer to the experts that</p> <p>24 are mineralogists or geologists to make that</p> <p>25 analysis. My opinion is that baby powder products</p>

<p style="text-align: right;">Page 66</p> <p>1 do not increase the risk of developing ovarian 2 cancer, regardless of what the constituent products 3 are in that product. 4 MS. CURRY: We've been going for an hour. 5 So when it's a good time to break, we'd like to take 6 one. 7 MS. GARBER: Sure. Just want to follow 8 up. 9 BY MS. GARBER: 10 Q So as to the constituents of the talcum 11 powder products, and what was or wasn't constituting 12 the constituents, you are going to defer to experts 13 in other areas; is that true? 14 MS. CURRY: Object to the form. 15 THE WITNESS: With respect to the 16 chemical composition of the product; yes. But not 17 with respect to the opinion that baby powder is not 18 associated with an increased risk of developing 19 ovarian cancer. 20 BY MS. GARBER: 21 Q I understand that. 22 And the same question with regard to the 23 presence of heavy metals, are you going to defer to 24 others as to whether or not Johnson & Johnson's 25 talcum powder products contained heavy metals?</p>	<p style="text-align: right;">Page 68</p> <p>1 powder is associated with developing ovarian cancer 2 would be borne out as showing a risk between 3 developing ovarian cancer in the use of the product. 4 What those individual constituents are, 5 I'm going to defer that analysis. But the opinion 6 that the baby powder as it stands with the 7 fragrances, with whatever else is in it, does not -- 8 is not associated with an increased risk of 9 developing ovarian cancer. I stand by that as my 10 opinion. 11 Q And the last question and then we'll 12 break. Same with regard to fibrous talc, are you 13 going to defer to experts as to whether or not 14 Johnson & Johnson's talcum powder products contained 15 fibrous talc? 16 MS. CURRY: Object to the form. 17 THE WITNESS: Yes. 18 MS. GARBER: Thanks. Let's take a break. 19 THE VIDEOGRAPHER: The time is now 10:32. 20 Going off the record. 21 (Break in the deposition taken at 10:33 a m.) 22 0o0 23 (The deposition resumed at 10:48 a m.) 24 0o0 25 THE VIDEOGRAPHER: Time is now 10:47.</p>
<p style="text-align: right;">Page 67</p> <p>1 A Yes. 2 Q Same question with regard to fragrances, 3 are you going to defer to others with regard to 4 whether Johnson & Johnson's talcum powder products 5 contained fragrances that may have been toxic or 6 carcinogens? 7 MS. CURRY: Object to the form. 8 THE WITNESS: So I'm not going to defer 9 that the product itself is associated with an 10 increased risk of developing ovarian cancer, meaning 11 the baby powder. But if there are constituent 12 fragrances in that product, I'm going to defer to 13 somebody whose analysis of the chemical composition 14 of that product is their field of expertise. 15 BY MS. GARBER: 16 Q So you know in looking at the label, 17 there's fragrance in the bottle; right? 18 A Well, it smells good, yeah. 19 Q It says that. And so what those 20 fragrances constitute and whether or not they are 21 toxic or carcinogenic, you're going to defer to 22 experts in that regard; is that true? 23 A No, that's not true. Because if those 24 fragrances were toxic or carcinogenic, then the 25 literature that is evaluating whether or not baby</p>	<p style="text-align: right;">Page 69</p> <p>1 Back on the record. 2 BY MS. GARBER: 3 Q Doctor, are you aware that Johnson & 4 Johnson enjoys about a 70 percent market share of 5 talcum powder products? 6 MS. CURRY: Object to the form. 7 THE WITNESS: I don't have any knowledge 8 of what their market share is. 9 BY MS. GARBER: 10 Q Do you know -- you understand what a risk 11 benefit assessment is in the context of medicine; 12 right? 13 A In the context of medicine? 14 Q Uh-huh. 15 A I've done risk benefit analyses, sure. 16 Q You're aware that there's no health 17 benefits for women to use defendant's talcum powder 18 products on their genitals, aren't you? 19 MS. CURRY: Object to the form. 20 THE WITNESS: I don't agree with that. 21 BY MS. GARBER: 22 Q You think there's medical benefits? 23 A I do. 24 Q Okay. You've seen literature that -- 25 peer-reviewed published literature that indicates</p>

Page 70

1 there's no medical benefits, haven't you?
 2 MS. CURRY: Object to the form.
 3 THE WITNESS: No, I have not.
 4 BY MS. GARBER:
 5 Q What were the medical benefits?
 6 A So there are some women that sweat a lot,
 7 and because they sweat, they can get candidal
 8 infections. And so some women like to apply baby
 9 powder products to their genital area to decrease
 10 the sweat so that they don't get candidal infection.
 11 Q If there's a medical benefit, then talcum
 12 powder is a medicine; right?
 13 A No. Patients use talcum powder in order
 14 to decrease the amount that they're sweating and
 15 that can result in them getting fewer candidal
 16 infections. It doesn't mean that it's a medicine.
 17 Q You understand that if there's medical
 18 benefits and patients are using it for medical
 19 purposes, then talcum powder isn't a cosmetic, but
 20 rather a medicine by way of regulatory oversight?
 21 Do you understand that?
 22 MS. CURRY: Object to the form.
 23 THE WITNESS: No. I don't agree with
 24 that. What you asked me is if patients use it for
 25 any sort of medical benefit. It's not dispensed as

Page 71

1 a medicine. It's not prescribed as a medicine. But
 2 women do use it in order to absorb whatever sweat
 3 they may have so that they don't get candidal
 4 infections or they don't have discomfort in the
 5 genital area from their sweat.
 6 BY MS. GARBER:
 7 Q Have you ever prescribed talcum powder
 8 products to your patients for medical benefit?
 9 A I've prescribed Nystatin powder, which
 10 does contain talc, to my patients, which does have a
 11 medical benefit of treating candidal infections.
 12 Q That is a medication; correct?
 13 A That's a medication.
 14 Q Talcum powder products are not?
 15 A So Nystatin powder does contain talc, so
 16 that is a talcum powder product.
 17 Q Nystatin powder is a medicine?
 18 A Nystatin powder is a medicine.
 19 Q Johnson & Johnson baby powder products
 20 are not a medicine?
 21 A That's correct.
 22 Q What is your definition of the phrase
 23 "latency period" in the context of ovarian cancer?
 24 A Latency period would be the time from --
 25 when we're talking about perhaps exposures to any

Page 72

1 particular agent, it would be the time from the
 2 exposure to the development of the disease.
 3 Q So in the context of the talcum powder
 4 product litigation, from the exposure to Johnson &
 5 Johnson's talcum powder products to the diagnosis of
 6 ovarian cancer?
 7 MS. CURRY: Object to the form.
 8 THE WITNESS: Well, I didn't say the
 9 diagnosis. I said the development of the disease.
 10 BY MS. GARBER:
 11 Q So when you say development, what do you
 12 mean? How do we know when the disease developed in
 13 the context of ovarian cancer?
 14 A So we don't necessarily know when it
 15 starts. We do know that ovarian cancer goes through
 16 various stages and you can diagnose it at various
 17 stages. Sometimes we catch it at stage 1, sometimes
 18 we catch it at stage 4.
 19 But in the general context of what a
 20 latency period is, it's from the time of exposure to
 21 the development of the disease.
 22 Q In the context of cohort studies, it's
 23 from -- the latency period is from the point of
 24 exposure to the point of diagnosis of the disease,
 25 isn't it?

Page 73

1 MS. CURRY: Object to the form.
 2 THE WITNESS: So in the cohort studies;
 3 yes, I think that's probably accurate.
 4 BY MS. GARBER:
 5 Q There are peer-reviewed published studies
 6 showing that ovarian cancer has a long latency
 7 period, reporting to be as long as 30 to 40 years,
 8 aren't there?
 9 MS. CURRY: Object to the form.
 10 THE WITNESS: There are some that show
 11 that. There are some that show other data.
 12 BY MS. GARBER:
 13 Q What is your opinion as to the latency
 14 period for ovarian cancer?
 15 A So I think the literature has shown some
 16 periods of 20 to 40 years. Since I don't really
 17 know what causes ovarian cancer and therefore I
 18 don't really know what is the incipient underlying
 19 events that have the cancer develop, I don't really
 20 have a specific sense other than to say I think it
 21 probably is reasonable that it's somewhere in
 22 between 20 to 40 years.
 23 Q And that's a range; correct?
 24 A That's correct.
 25 Q Do you agree with the statement, if

<p style="text-align: right;">Page 74</p> <p>1 talcum powder is a potential carcinogen for ovarian 2 cancer, it is likely that there is a long latency 3 period between exposure and development of the 4 disease? 5 MS. CURRY: Object to the form. 6 THE WITNESS: As a general statement, I 7 don't know what that word "long" necessarily means, 8 but I think as a general statement I would agree 9 with that statement. 10 BY MS. GARBER: 11 Q Is it true that for asbestos the latency 12 period is at least 25 years, according to 13 peer-reviewed published studies? 14 MS. CURRY: Object to the form. 15 THE WITNESS: So I think in the IARC 16 monograph that looked at heavy occupational exposure 17 of patients to -- I should say subjects -- of 18 subjects to asbestos, there was one study that 19 tracked when the subjects were exposed to the 20 asbestos and then looked at how many years later 21 they were diagnosed with ovarian cancer, and I do 22 believe that range was somewhere between 20 to 23 25 years. 24 However, I think there are a lot of 25 problems with the asbestos studies in general.</p>	<p style="text-align: right;">Page 76</p> <p>1 association. 2 Q We will turn to that shortly. But 3 thank you for that. 4 Do you have an opinion, then, as to the 5 latency period for asbestos, and ovarian cancer? 6 A So again, I don't necessarily agree with 7 IARC's conclusions about developing ovarian cancer 8 with asbestos exposure, but as documented in the 9 articles that IARC cites, the latency period 10 reported is 20 to 25 years. 11 Q And you mentioned the Camargo paper, you 12 read that one? 13 A Yes. 14 Q It's on your reference list? 15 A Yes. 16 Q And didn't that study show a 17 statistically -- showed a statistically significant 18 association after 25 years of follow up? 19 MS. CURRY: Object to the form. If you 20 need to see the article, I have a copy. 21 THE WITNESS: Sure. I'd be happy to take 22 a look at it. 23 MS. GARBER: Okay. Well, so first thing 24 we're going to do is we're going to make sure we 25 don't have speaking objections, Ms. Curry. And I'm</p>
<p style="text-align: right;">Page 75</p> <p>1 BY MS. GARBER: 2 Q Did you do a comprehensive literature 3 review of asbestos and ovarian cancer? 4 MS. CURRY: Object to the form. 5 THE WITNESS: I read the studies that are 6 listed in the IARC Monograph. 7 BY MS. GARBER: 8 Q You read each and every one of those 9 studies that's listed in the IARC Monograph? 10 A Yes, as pertains to asbestos and ovarian 11 cancer. 12 Q And which monograph are you speaking of? 13 A The 2012. 14 Q And how many studies was that, by your 15 recollection? 16 A So IARC drew their conclusions on the 17 basis of five studies that looked at heavy 18 occupational exposure and the risk of developing 19 ovarian cancer. There have been other studies after 20 that as well that I have read, including Reed, 21 including Camargo, and looked at the risk of 22 developing ovarian cancer and asbestos exposure in 23 the heavy occupational setting. 24 There also were other studies that looked 25 at environmental exposure and did not find any such</p>	<p style="text-align: right;">Page 77</p> <p>1 not going to pull out that article right now. We'll 2 get to that when I want to get to that. 3 BY MS. GARBER: 4 Q You've been designated as an expert 5 witness by Johnson & Johnson in the talcum powder 6 product litigation in the MDL; right? 7 A Yes. 8 Q You understand that we are here to take 9 your deposition, to get all of your opinions and the 10 bases for those opinions so we can prepare for 11 briefing, hearing, and trial. 12 Do you understand that? 13 A Yes. 14 Q Did you see the Notice of Deposition that 15 was served with regard to your deposition? 16 A Yes. 17 Q When did you see that? 18 A I believe last week sometime. 19 Q Have you -- did you understand that in 20 the Notice of Deposition there was a request for 21 documents for you to bring to today's deposition, or 22 actually to provide five days before today's 23 deposition? Did you notice that? 24 A I read the deposition notice and I know 25 that there were a number of requests, and I believe</p>

<p>Page 78</p> <p>1 that -- I don't have any documents to provide you 2 with. I think my CV was already provided. 3 MS. CURRY: Just for the record, the 4 Notice of Deposition was actually received by 5 Johnson & Johnson just six business days ago and the 6 responses are subject to the objections that were 7 filed on behalf of Johnson & Johnson. 8 (C. Saenz Exhibit 3 was marked for 9 identification.) 10 MS. GARBER: I'm going to mark as 11 Exhibit 3 the Notice of Deposition. 12 THE WITNESS: Thank you. 13 BY MS. GARBER: 14 Q Turning, Dr. Saenz, to page five of the 15 notice. Those are the documents that we asked you 16 to produce that you have reviewed this list. 17 A Okay. 18 Q Have you? 19 A Yes. 20 Q In connection with the request number 21 two, item B, have you produced all of the invoices 22 for the expert work that you've done so far? 23 MS. CURRY: Subject to the objections 24 that were produced on behalf -- 25 MS. GARBER: I'll give you an ongoing</p>	<p>Page 80</p> <p>1 issue of subject to the objections, because the 2 objections made clear that the documents that were 3 produced were with respect to the MDL talcum powder 4 litigation and not all talcum powder litigation. 5 So I was just making that clarification 6 so that you know which documents were actually 7 produced and why. 8 BY MS. GARBER: 9 Q Dr. Saenz, do you have any communications 10 in connection with any of the study authors 11 concerning talc or talcum powder products in ovarian 12 cancer? 13 A With what studies? 14 Q Any of the published studies. Have you 15 communicated with any of the study authors? 16 A Oh. So I don't know that I can answer 17 that specifically, because I don't know if over the 18 course of my career I've ever communicated with 19 anybody that's ever been listed. I mean, I 20 certainly know some of them professionally, so at 21 some point, I would have communicated with them. 22 Q Since you've been an expert in the MDL, 23 have you communicated with any study authors? 24 A I'm sure I have. Again, because the 25 world of OB-GYN oncology is a rather small world and</p>
<p>Page 79</p> <p>1 objection. 2 MS. CURRY: Thank you. 3 THE WITNESS: Yes. 4 BY MS. GARBER: 5 Q Have you produced all invoices and 6 payments in connection with your talcum powder 7 products work in general? 8 A We're -- 9 MS. CURRY: Object to the form. 10 THE WITNESS: With my -- everything that 11 I've invoiced has been produced. 12 BY MS. GARBER: 13 Q Including from other litigations? 14 MS. SHARKO: You need to look at the 15 objections we served. This isn't fair to just look 16 at the note. We responded -- although it came very 17 late, we responded yesterday. 18 MS. GARBER: Ms. Sharko, with all due 19 respect, I think we're having one attorney at a time 20 represent the witness. I'm sure Ms. Curry is very 21 capable of objecting. 22 MS. SHARKO: I wish you had been at all 23 the other depositions where three of you all were 24 talking, but I understand your point. 25 MS. CURRY: This is why I was raising the</p>	<p>Page 81</p> <p>1 so some of the people on some of the studies are in 2 the same professional organizations that I'm in. 3 So I'm sure I've had professional 4 communications. 5 Q Have you had professional communications 6 with any of the study authors in connection with 7 talcum powder products? 8 A Oh. No. 9 Q Thank you. Have you had any 10 communications with the Society of Gynecologic 11 Oncology in connection with talcum powder products 12 since you've been retained as an expert witness in 13 any talcum powder product litigation? 14 A Specifically with regard to this issue? 15 Q Yes. 16 A No. 17 Q Same question as to have you had any 18 communications with regard to talcum powder 19 litigation with the American Congress of Obstetrics 20 and Gynecology? 21 A With respect to this particular issue, 22 no. 23 Q And when you say with respect to this 24 particular issue, what do you mean so I know? 25 A With respect to talcum powder litigation,</p>

<p style="text-align: right;">Page 82</p> <p>1 no.</p> <p>2 Q Talcum powder products and the risk of</p> <p>3 ovarian cancer?</p> <p>4 A Correct.</p> <p>5 Q Thank you. Turning to the objections</p> <p>6 that were issued in this matter and the documents</p> <p>7 that are attached, I want to review those briefly</p> <p>8 with you; okay. Do you have a copy?</p> <p>9 A No, I don't.</p> <p>10 THE WITNESS: Thank you so much.</p> <p>11 MS. GARBER: We'll mark that as</p> <p>12 Exhibit 4.</p> <p>13 (C. Saenz Exhibit 4 was marked for</p> <p>14 identification.)</p> <p>15 BY MS. GARBER:</p> <p>16 Q And the first document looks to be on the</p> <p>17 UCSD Moores Cancer Center letterhead signed by you?</p> <p>18 A I'm sorry, ma'am, what page are we on?</p> <p>19 Q Third from the last.</p> <p>20 A Okay.</p> <p>21 Q Is that an invoice?</p> <p>22 A Yes.</p> <p>23 Q We already spoke about that earlier,</p> <p>24 that's reflecting the work that was done by you from</p> <p>25 December 18th to February 2019?</p>	<p style="text-align: right;">Page 84</p> <p>1 reviewed since I submitted my report.</p> <p>2 Q And so is it true that from the point</p> <p>3 that you issued your report to today, the only</p> <p>4 documents you reviewed in connection with your</p> <p>5 opinions are those listed here at the supplement to</p> <p>6 the materials reviewed by Dr. Cheryl Saenz?</p> <p>7 MS. CURRY: Object to the form.</p> <p>8 THE WITNESS: So no, because I actually</p> <p>9 did a little bit more reading last evening. So I</p> <p>10 haven't informed anybody of that, other than what I</p> <p>11 did myself.</p> <p>12 BY MS. GARBER:</p> <p>13 Q Turning to that soon. So you knew where</p> <p>14 I was going. But what did you read last night?</p> <p>15 A Last evening I reread the Penninkilampi</p> <p>16 meta-analysis, and I pulled online the reference</p> <p>17 where they talk about ovarian cancer -- sorry,</p> <p>18 ovarian epithelial cells lacking COX-1 and COX-2,</p> <p>19 and therefore, I went to see that article to see if</p> <p>20 that was actually quoted properly in the</p> <p>21 Penninkilampi study.</p> <p>22 And then I was aware of some other</p> <p>23 studies just from personal knowledge that actually</p> <p>24 did document that COX-1 and COX-2 are in ovarian</p> <p>25 cancer cells, so I re-reviewed those myself just to</p>
<p style="text-align: right;">Page 83</p> <p>1 A Correct.</p> <p>2 Q And at a rate of \$750 an hour?</p> <p>3 A That's correct.</p> <p>4 Q If we turn to the next document, it is</p> <p>5 also on UCSD Medical Center Moores Cancer Center</p> <p>6 letterhead; correct?</p> <p>7 A What's the title of the document?</p> <p>8 Q Legal consultation fee schedule.</p> <p>9 A Okay; yes, I'm there.</p> <p>10 Q Did you draft this document?</p> <p>11 A Yes.</p> <p>12 Q What is the nature of this document?</p> <p>13 A This is my fee schedule as of October</p> <p>14 of 2016, I believe, is the last time I revised it.</p> <p>15 Q And what does out of town travel fees</p> <p>16 mean?</p> <p>17 A It means I pick up, I leave San Diego</p> <p>18 County, and I go someplace else.</p> <p>19 Q The third document that was produced is</p> <p>20 a -- is titled "Supplement to Materials Reviewed By</p> <p>21 Dr. Cheryl Saenz"; is that correct?</p> <p>22 A Yes.</p> <p>23 Q Did you draft this document?</p> <p>24 A I didn't do the actual typing, but I did</p> <p>25 send an email to Ms. Curry about things that I had</p>	<p style="text-align: right;">Page 85</p> <p>1 make sure that my recollection was accurate.</p> <p>2 Q What were those? What were the titles of</p> <p>3 those studies?</p> <p>4 A So I don't recall the Penninkilampi</p> <p>5 title, the one that's referenced in Penninkilampi,</p> <p>6 but I think it was reference 27. I'm happy to show</p> <p>7 you if you have the article, but I think it was</p> <p>8 reference 27 in the Penninkilampi.</p> <p>9 Then the other two articles that I read</p> <p>10 were actually out of Dr. Khabele's lab, and they</p> <p>11 look at the presence of COX-1 and COX-2 in ovarian</p> <p>12 cancer cells.</p> <p>13 And I had read that actually to -- like,</p> <p>14 one was published last year and one was published a</p> <p>15 few years ago. I had read that before and I just</p> <p>16 re-reread them. But do I believe that Dr. Khabele</p> <p>17 is the senior author, but -- I'm sorry, I don't</p> <p>18 remember the title, but I think that Dr. Khabele was</p> <p>19 the senior author on those papers.</p> <p>20 Q How do you spell Khabele?</p> <p>21 A K-H-A-B-E LE, and her first name is</p> <p>22 Dineo, D-I-N-E-O.</p> <p>23 Q Do you know the second study author's</p> <p>24 name?</p> <p>25 A Well, Dr. Khabele was senior author on</p>

<p style="text-align: right;">Page 86</p> <p>1 both of those, so she's actually the last author.</p> <p>2 Q Do you remember the first author?</p> <p>3 A I don't, I'm sorry.</p> <p>4 Q That's okay. So there were two papers by</p> <p>5 the Khabele lab?</p> <p>6 A Yes.</p> <p>7 Q What was the upshot of their findings?</p> <p>8 A That there is expression of COX-1 and</p> <p>9 COX-2 in ovarian cancer cells, as well as production</p> <p>10 of mRNA, particularly for COX-1.</p> <p>11 The Penninkilampi study -- well, it</p> <p>12 wasn't the Penninkilampi study, but it was the</p> <p>13 reference in Penninkilampi, they actually did find</p> <p>14 expression of COX-1 and COX-2 proteins in the</p> <p>15 ovarian cancer cell lines that they looked at. And</p> <p>16 so Penninkilampi actually was incorrect in the way</p> <p>17 that they were referencing that study. That's why I</p> <p>18 looked at it.</p> <p>19 Q So your take-away is that the</p> <p>20 Penninkilampi paper miscited whether there's</p> <p>21 expression of COX-1 and COX-2 in epithelial ovarian</p> <p>22 cells?</p> <p>23 MS. CURRY: Object to the form.</p> <p>24 THE WITNESS: Well, the paper that they</p> <p>25 cited, I think they cited it correctly, but I think</p>	<p style="text-align: right;">Page 88</p> <p>1 department, and so I knew her research and I knew</p> <p>2 she had shown that COX was in ovarian cancer cells,</p> <p>3 so it seemed that like strange to me that</p> <p>4 Penninkilampi said that it wasn't there.</p> <p>5 So that's why I went back in and wanted</p> <p>6 to verify that.</p> <p>7 Q Did you do a comprehensive literature</p> <p>8 review on the issue of whether epithelial ovarian</p> <p>9 cancer express -- I'm sorry, epithelial ovarian</p> <p>10 cells express COX-1 and COX-2?</p> <p>11 MS. CURRY: Object to the form.</p> <p>12 THE WITNESS: So I read those three</p> <p>13 papers. I had read Dr. Khabele's papers before, but</p> <p>14 I read these papers last evening and read them</p> <p>15 thoroughly. So I wouldn't say I've read every</p> <p>16 article ever published on it, but I certainly read</p> <p>17 the paper that Penninkilampi referenced and I read</p> <p>18 Dr. Khabele's work, which I think actually is some</p> <p>19 of the largest volume of work given the tissue</p> <p>20 microarray that she studies and how many different</p> <p>21 specimens she actually looked at it.</p> <p>22 BY MS. GARBER:</p> <p>23 Q And based on your review of the three</p> <p>24 studies, are you going to give an opinion whether or</p> <p>25 not you believe and it's your opinion whether</p>
<p style="text-align: right;">Page 87</p> <p>1 they misstated the results of that study, yes.</p> <p>2 BY MS. GARBER:</p> <p>3 Q So do you have opinion, Doctor, based on</p> <p>4 your research as to whether epithelial ovarian cells</p> <p>5 express COX-1 and COX-2?</p> <p>6 A So that gets to the point of where I</p> <p>7 think Penninkilampi misrepresented the conclusions</p> <p>8 of the study, because Penninkilampi stated that</p> <p>9 ovarian epithelium doesn't have COX-1 or COX-2. But</p> <p>10 the study they cited wasn't on normal ovarian</p> <p>11 epithelium, it was actually on cancer cells, and the</p> <p>12 cancer cells actually did have expression of COX-1</p> <p>13 and COX-2.</p> <p>14 Q Why did you go back and look at that in</p> <p>15 particular?</p> <p>16 A Because I was reading the Penninkilampi</p> <p>17 study again, and it's meta-analysis that's focused</p> <p>18 on by many of your experts, and I felt it was</p> <p>19 important to the whole theory of chronic</p> <p>20 inflammation and why NSAIDS may or may not show a</p> <p>21 decreased risk of ovarian cancer. The literature on</p> <p>22 that is very inconsistent.</p> <p>23 I also am very familiar with the work in</p> <p>24 Dr. Khabele's lab because -- well, she once</p> <p>25 interviewed for a division director at our</p>	<p style="text-align: right;">Page 89</p> <p>1 epithelial ovarian cells express COX-1 and COX-2?</p> <p>2 A Yes.</p> <p>3 Q You're going to say they don't?</p> <p>4 A No, I'm going to say they do.</p> <p>5 Q They do --</p> <p>6 A They do express COX-1 and COX.</p> <p>7 Q So you have not produced all documents</p> <p>8 that relate to your compensation for expert work in</p> <p>9 this matter; correct?</p> <p>10 MS. CURRY: Object to the form.</p> <p>11 THE WITNESS: With respect to this MDL</p> <p>12 work, this particular matter, I have. I've only</p> <p>13 invoiced the one invoice.</p> <p>14 BY MS. GARBER:</p> <p>15 Q That was a bad question.</p> <p>16 You have not produced all documents that</p> <p>17 relate to your compensation for expert work done in</p> <p>18 the talcum powder litigation; correct?</p> <p>19 MS. CURRY: Object to the form. It's the</p> <p>20 subject of our objections.</p> <p>21 THE WITNESS: I've only produced the</p> <p>22 invoice for this particular matter.</p> <p>23 BY MS. GARBER:</p> <p>24 Q With regard to the supplement to</p> <p>25 materials reviewed by Dr. Cheryl Saenz, did you</p>

<p style="text-align: right;">Page 90</p> <p>1 review any other expert reports?</p> <p>2 MS. CURRY: Object to the form.</p> <p>3 THE WITNESS: On the defense side or the</p> <p>4 plaintiff side?</p> <p>5 MS. GARBER: Either side.</p> <p>6 THE WITNESS: So, yes, but I think that's</p> <p>7 listed in the materials reviewed. This is only the</p> <p>8 listing of the defense expert reports that I</p> <p>9 reviewed subsequent to submitting my report in the</p> <p>10 original materials reviewed list.</p> <p>11 BY MS. GARBER:</p> <p>12 Q What was the nature of reviewing those</p> <p>13 particular expert reports? Did you ask for them?</p> <p>14 Were they provided?</p> <p>15 MS. CURRY: Object to the form.</p> <p>16 THE WITNESS: The ones on the supplement</p> <p>17 lists?</p> <p>18 MS. GARBER: Yes.</p> <p>19 THE WITNESS: Okay. The ones on the</p> <p>20 supplement list, I've actually been provided with</p> <p>21 these expert reports, and I picked these particular</p> <p>22 ones because I wanted -- after my report was</p> <p>23 submitted, I felt that it was important for me to</p> <p>24 see what the other expert said with regards to</p> <p>25 things that I had actually given opinions on as</p>	<p style="text-align: right;">Page 92</p> <p>1 A No.</p> <p>2 Q Have you ever spoken with Dr. Holcombe</p> <p>3 about this litigation?</p> <p>4 A No.</p> <p>5 Q Did you conduct any research in</p> <p>6 connection with your expert opinion?</p> <p>7 MS. CURRY: Object to the form.</p> <p>8 BY MS. GARBER:</p> <p>9 Q In other words, did you do a literature</p> <p>10 search on PubMed or Medline?</p> <p>11 A Oh. Yes, I often -- particularly as I</p> <p>12 was reading an article, if I felt that there was</p> <p>13 something that was important in one of the reference</p> <p>14 lists for an article that I was reading, then I</p> <p>15 would go do a lit search to find that article and</p> <p>16 read that as well.</p> <p>17 But yes, I've done quite an extensive</p> <p>18 literature search.</p> <p>19 Q Did you ever do any general searches, for</p> <p>20 instance, talcum powder products and ovarian cancer,</p> <p>21 or was it just to find other papers based on the</p> <p>22 papers you had previously read?</p> <p>23 MS. CURRY: Object to the form.</p> <p>24 THE WITNESS: I've done all of that.</p> <p>25 ///</p>
<p style="text-align: right;">Page 91</p> <p>1 well.</p> <p>2 BY MS. GARBER:</p> <p>3 Q Prior to finalizing and signing your</p> <p>4 expert report, in the MDL, did you review any draft</p> <p>5 reports of any of the defense experts?</p> <p>6 A No.</p> <p>7 Q Did you ever speak with any of the</p> <p>8 experts?</p> <p>9 A About --</p> <p>10 MS. CURRY: Object to the form.</p> <p>11 THE WITNESS: About this matter?</p> <p>12 MS. GARBER: Yes.</p> <p>13 THE WITNESS: No.</p> <p>14 BY MS. GARBER:</p> <p>15 Q After you issued your MDL report, have</p> <p>16 you spoken with any of the defense experts about</p> <p>17 this litigation?</p> <p>18 A No.</p> <p>19 Q Have you ever spoken with Dr. Swisher</p> <p>20 about this litigation?</p> <p>21 A No.</p> <p>22 Q Have you ever spoken with Dr. Huh about</p> <p>23 this litigation?</p> <p>24 A Warner?</p> <p>25 Q Yes?</p>	<p style="text-align: right;">Page 93</p> <p>1 BY MS. GARBER:</p> <p>2 Q Did counsel in the MDL provide for you</p> <p>3 any published literature for you to review?</p> <p>4 A Other than that flash drive that we</p> <p>5 originally talked back in November of 2016, no.</p> <p>6 Oh, ma'am, I'm sorry. For the sake of</p> <p>7 the completeness, I have received a copy of that</p> <p>8 Health Canada assessment which was not available to</p> <p>9 me online, and also the Taher article, which has not</p> <p>10 been published. And it's in my materials reviewed,</p> <p>11 but I believe that I received one or two of the</p> <p>12 abstracts from Dr. Saed's lab that have yet to be</p> <p>13 presented.</p> <p>14 So, sorry, that was provided for me. But</p> <p>15 I asked for those materials. They weren't provided</p> <p>16 to me without me reading about them I think in</p> <p>17 plaintiff's experts' depositions or reports and then</p> <p>18 I asked to see them. Sorry about that.</p> <p>19 Q Between when you were first retained in</p> <p>20 2016 and were given the flash drive and completing</p> <p>21 your expert report in the MDL, you were not provided</p> <p>22 any published literature by Johnson & Johnson</p> <p>23 lawyers. Is that a true statement?</p> <p>24 A Other than what we've just discussed?</p> <p>25 Q I'm trying to narrow down before your</p>

<p style="text-align: right;">Page 94</p> <p>1 expert report was issued.</p> <p>2 A Oh, before it was issued?</p> <p>3 Q Yes.</p> <p>4 A But I just listed those things. So I did</p> <p>5 receive those before it was issued.</p> <p>6 Q Okay. We're -- I'm going to mark your</p> <p>7 report in a minute. But before your expert report</p> <p>8 was issued, you had received some Dr. Saed</p> <p>9 abstracts, the Taher meta-analysis and the Health</p> <p>10 Canada review?</p> <p>11 A The Health Canada summary, yeah, the</p> <p>12 assessment; right. Yes, before my report was</p> <p>13 issued.</p> <p>14 Q Which abstracts did you receive in</p> <p>15 connection with Dr. Saed's work?</p> <p>16 A I'd have to look at my expert report to</p> <p>17 see exactly because they're listed there in the</p> <p>18 materials reviewed.</p> <p>19 MS. GARBER: Let's mark the expert</p> <p>20 report.</p> <p>21 (C. Saenz Exhibit 5 was marked for</p> <p>22 identification.)</p> <p>23 MS. GARBER: We'll mark the expert report</p> <p>24 of Cheryl Saenz dated February 25th, 2019, as</p> <p>25 Exhibit 5.</p>	<p style="text-align: right;">Page 96</p> <p>1 A These are all the references that I made</p> <p>2 reference to in my report.</p> <p>3 Q So these are the references that were</p> <p>4 cited to in the body of your expert report?</p> <p>5 A Right. These are the -- right, exactly.</p> <p>6 Q Then if we turn to 40 through 42, what is</p> <p>7 the nature of those documents titled "Additional</p> <p>8 Materials Reviewed By Dr. Cheryl Saenz"?</p> <p>9 A So these are other articles that I have</p> <p>10 read over the time period that I have been giving</p> <p>11 opinions in the talc litigation matters, but that I</p> <p>12 didn't necessarily reference in my report.</p> <p>13 Q I notice those are listed alphabetically,</p> <p>14 are they not?</p> <p>15 A Yes.</p> <p>16 Q I don't see any reference to any of</p> <p>17 Dr. Saenz' work; is that true?</p> <p>18 A I am Dr. Saenz.</p> <p>19 Q I'm sorry. I don't see any reference to</p> <p>20 Dr. Saed's work. Do you?</p> <p>21 A So if you look on page 33, reference 21,</p> <p>22 Nicole Fletcher is first author on one of his works.</p> <p>23 That's actually his work.</p> <p>24 Q With regard -- I was referencing the</p> <p>25 second grouping. Do you cite any of Dr. Saed's</p>
<p style="text-align: right;">Page 95</p> <p>1 Do you need one?</p> <p>2 MS. CURRY: No, I have one.</p> <p>3 BY MS. GARBER:</p> <p>4 Q Doctor, let's turn in Exhibit 5 of your</p> <p>5 expert report --</p> <p>6 MS. CURRY: Actually, can I just ask you</p> <p>7 one thing. The copy that Dr. Saenz has that's been</p> <p>8 marked as an official exhibit is not in color, but</p> <p>9 there is some color in the original report.</p> <p>10 Do you want to mark the color version or</p> <p>11 swap it out?</p> <p>12 MS. GARBER: If you want to -- do you</p> <p>13 have a color copy?</p> <p>14 MS. CURRY: I do.</p> <p>15 MS. GARBER: Sure.</p> <p>16 THE WITNESS: I'm sorry, what page,</p> <p>17 ma'am?</p> <p>18 BY MS. GARBER:</p> <p>19 Q If we turn to page 32 of your report.</p> <p>20 A Yes.</p> <p>21 Q There is a document that spans from</p> <p>22 page 32 to 39 that was titled "References"?</p> <p>23 A Yes.</p> <p>24 Q Can you tell me what the nature of that</p> <p>25 document is?</p>	<p style="text-align: right;">Page 97</p> <p>1 abstracts?</p> <p>2 A No, because I do in the report. That's</p> <p>3 why it's in the report. That's why it's listed</p> <p>4 there.</p> <p>5 Q I think you told me several abstracts. I</p> <p>6 don't see -- or a couple of abstracts. I don't see</p> <p>7 more than one.</p> <p>8 A I can't remember the name of his other</p> <p>9 first author. There's Fletcher and then there's --</p> <p>10 I can't remember who else he published with.</p> <p>11 Q Did you read Dr. Saed's 2019 publication</p> <p>12 with regard to talc and ovarian cancer molecular</p> <p>13 mechanisms?</p> <p>14 A No, I don't believe that I did. I</p> <p>15 believe that I read his deposition testimony and his</p> <p>16 expert report. So I would have learned what I</p> <p>17 learned about what he did from his expert report as</p> <p>18 well as his deposition testimony.</p> <p>19 Q So I'm clear, you have not read his 2019</p> <p>20 publication; is that true?</p> <p>21 A I don't believe that I have.</p> <p>22 Q It isn't your testimony, is it,</p> <p>23 Dr. Saenz, that by reading his deposition and expert</p> <p>24 report, you thereby know what is in his peer</p> <p>25 reviewed and published publications?</p>

<p style="text-align: right;">Page 98</p> <p>1 MS. CURRY: Object to the form.</p> <p>2 THE WITNESS: I've not read the</p> <p>3 publication from 2019. I have read his expert</p> <p>4 report wherein he describes the experiments he did,</p> <p>5 I believe, for that publication. But no, I have not</p> <p>6 read the 2019 publication.</p> <p>7 BY MS. GARBER:</p> <p>8 Q You do make comments about his</p> <p>9 publication in your expert report?</p> <p>10 A The one --</p> <p>11 MS. CURRY: Object to the form.</p> <p>12 THE WITNESS: -- that is cited in my</p> <p>13 report; correct.</p> <p>14 BY MS. GARBER:</p> <p>15 Q Did you ask Johnson & Johnson to provide</p> <p>16 you with any documents?</p> <p>17 MS. CURRY: Objection to the form.</p> <p>18 THE WITNESS: What do you mean by</p> <p>19 "documents"?</p> <p>20 BY MS. GARBER:</p> <p>21 Q Any. Did you ask for any documents</p> <p>22 whatsoever from Johnson & Johnson?</p> <p>23 A Well, yes, we've already covered I asked</p> <p>24 for the Health Canada assessment and I asked for the</p> <p>25 Taher report, and I believe I asked for one of the</p>	<p style="text-align: right;">Page 100</p> <p>1 Q Why not?</p> <p>2 A I didn't believe that they were important</p> <p>3 to my opinion. I don't know where they would come</p> <p>4 from. They're not peer-reviewed literature and my</p> <p>5 opinion is based on my experience, my treating</p> <p>6 patients with ovarian cancer, as well as assessing</p> <p>7 people, and the risk factors and a review of the</p> <p>8 peer-reviewed literature.</p> <p>9 Q What Johnson & Johnson, the defendant,</p> <p>10 was saying about the science was not important to</p> <p>11 you, Dr. Saenz?</p> <p>12 MS. CURRY: Object to the form.</p> <p>13 THE WITNESS: So I wouldn't know the</p> <p>14 context of that. What's important to me in</p> <p>15 assessing whether or not application of talcum</p> <p>16 powder products in the perineum is increasing the</p> <p>17 risk of ovarian cancer is reading the peer-reviewed</p> <p>18 literature to see if that's substantiated by that.</p> <p>19 BY MS. GARBER:</p> <p>20 Q For the expert reports that are listed in</p> <p>21 your reference materials, all of them, all three</p> <p>22 lists, did you read every word of those reports?</p> <p>23 A Can you reference me which page we're</p> <p>24 looking at now? Are we looking at the supplemental</p> <p>25 list or --</p>
<p style="text-align: right;">Page 99</p> <p>1 abstracts from Dr. Saed to take a look at that.</p> <p>2 Q Which abstract was that?</p> <p>3 A I think it's the one that's referenced</p> <p>4 there as reference 21.</p> <p>5 Q How did you know to ask for that?</p> <p>6 A Because I read his report and saw where</p> <p>7 he talked about that. But I also read the reports</p> <p>8 of some of plaintiff's gynecological oncology</p> <p>9 experts where they reference that he talked about</p> <p>10 rising levels of CA 125 as a result of talc</p> <p>11 treatment of ovarian cancer cells.</p> <p>12 Q How did you know to ask for the Taher</p> <p>13 paper?</p> <p>14 A Because that was discussed in, I believe,</p> <p>15 the depositions of some of plaintiff's experts.</p> <p>16 Q How did you know to ask for the Health</p> <p>17 Canada assessment?</p> <p>18 A Again, the same thing. I believe that</p> <p>19 was discussed in some of plaintiff's experts</p> <p>20 depositions.</p> <p>21 Q Did you ask Johnson & Johnson for any</p> <p>22 internal documents?</p> <p>23 A Internal to Johnson & Johnson?</p> <p>24 Q Yes.</p> <p>25 A No.</p>	<p style="text-align: right;">Page 101</p> <p>1 Q All three.</p> <p>2 A -- the report?</p> <p>3 Q Well, actually, it would just be the --</p> <p>4 let's see what you called it -- additional</p> <p>5 materials. Have you -- which is at page 40,</p> <p>6 attached to your expert report, have you read every</p> <p>7 word of those expert reports?</p> <p>8 A Yes.</p> <p>9 Q Sorry. Okay. Have you read every word</p> <p>10 of the deposition transcript of the witnesses listed</p> <p>11 on page 40?</p> <p>12 A Yes.</p> <p>13 Q And similarly, have you read every word</p> <p>14 of the expert reports that is listed on the</p> <p>15 supplement to materials review by Dr. Cheryl Saenz?</p> <p>16 A Yes.</p> <p>17 Q You read Dr. Crowley's deposition</p> <p>18 testimony; right?</p> <p>19 A Yes.</p> <p>20 Q What did you glean from his deposition</p> <p>21 testimony?</p> <p>22 MS. CURRY: Object to the form.</p> <p>23 THE WITNESS: What did I glean?</p> <p>24 MS. GARBER: Uh-huh.</p> <p>25 THE WITNESS: I gleaned that I don't</p>

<p style="text-align: right;">Page 102</p> <p>1 think he necessarily understands that the vaginal 2 mucosa and the eye mucosa are the same. 3 BY MS. GARBER: 4 Q And you've made reference to that in 5 your expert report, haven't you? 6 A Yes. 7 Q Did you glean anything else from reading 8 his testimony? 9 MS. CURRY: Object to the form. 10 THE WITNESS: Not that I wanted to remark 11 on. 12 BY MS. GARBER: 13 Q Do you have any criticisms of his expert 14 report other than with regard to the vaginal mucosa? 15 A Not that I know. 16 MS. CURRY: Object to the form. 17 THE WITNESS: Not that I intend to give. 18 BY MS. GARBER: 19 Q What did you glean from the testimony of 20 Dr. Saed? 21 MS. CURRY: Object to the form. 22 THE WITNESS: I felt that based on his -- 23 I believe that based on his deposition testimony, 24 that there were a lot of irregularities in the 25 research that he conducted. I don't believe that</p>	<p style="text-align: right;">Page 104</p> <p>1 cancer cells causes changes in the molecular biology 2 of those cells that leads to ovarian cancer and I 3 don't believe that the reports that -- that the 4 reports of his data, the way that he puts them 5 forth, actually show that. 6 BY MS. GARBER: 7 Q But you make that statement not having 8 read all his data, don't you? 9 MS. CURRY: Object to the form. 10 THE WITNESS: I read his report and I 11 read his deposition and I read at least one of the 12 papers from Fletcher and Saed, and I read definitely 13 references to him in other expert plaintiff's 14 reports. 15 BY MS. GARBER: 16 Q Doctor, from reading his expert report 17 and from reading his two depositions; right? 18 A There were two volumes to his deposition; 19 correct. 20 Q You understood that he published a study 21 whereby he conducted an experiment with talc and the 22 cellular response, but yet you didn't ask for that 23 study? You didn't ask to review that study itself? 24 MS. CURRY: Object to the form. 25 THE WITNESS: No, I read his testimony</p>
<p style="text-align: right;">Page 103</p> <p>1 the results as he stated them from his work 2 necessarily support the hypothesis that chronic 3 inflammation leads to the development of ovarian 4 cancer. 5 BY MS. GARBER: 6 Q And with regard to your prior statement, 7 "I don't believe that the results as he stated them 8 from his work necessarily support the hypothesis 9 that chronic inflammation leads to the development 10 of ovarian cancer," is limited to the context of his 11 study that appears at reference 21? 12 MS. CURRY: Object to the form. 13 THE WITNESS: No. I believe that what 14 you asked me about was his -- what I gleaned from 15 his deposition testimony and so I was commenting on 16 that. 17 I think that Dr. Saed is mentioned in 18 many different places, many different expert reports 19 and so to some extent, it gets confusing to me as to 20 what the source for each and every one of these 21 things is. 22 Sometimes I saw it in expert plaintiff's 23 reports or their deposition testimony. But from 24 Dr. Saed's deposition testimony, I believe that he 25 talks about how his treatment of talc to the ovarian</p>	<p style="text-align: right;">Page 105</p> <p>1 where he talked about those things and he had his 2 notebooks in front of him. And I also read his 3 report, because he even discussed in his deposition 4 that the science that was in his report is the 5 experiments that he then went on to publish. 6 BY MS. GARBER: 7 Q I see. As a scientist, you just read a 8 deposition, you don't bother to consult the data. 9 Is that how it works? 10 MS. CURRY: Objection. Argumentative. 11 THE WITNESS: No. 12 BY MS. GARBER: 13 Q Don't you think the best source of 14 understanding Dr. Saed's work is to look at the data 15 itself, Dr. Saenz? 16 MS. CURRY: Object to the form. 17 THE WITNESS: I did look at the data from 18 the Fletcher and Saed paper and then -- 19 BY MS. GARBER: 20 Q But you didn't look at the 2019 data, did 21 you, Dr. Saenz? 22 A Ma'am, I wasn't finished with my 23 response. 24 Q I'm sorry. Go ahead and finish. 25 A I look at what Dr. Saed's report was and</p>

<p style="text-align: right;">Page 106</p> <p>1 there was data in that report; that is his expert 2 report. He provided data in that expert report as 3 to the experiments that he had done and that's what 4 I looked at. 5 Q For your critique, Doctor, don't you 6 think it would be fair for you to look at the source 7 data rather than rely on his deposition testimony 8 about those data? 9 Isn't the direct data more reliable than 10 his deposition about the data? 11 MS. CURRY: Object to the form. 12 THE WITNESS: I didn't say his 13 deposition. I said his report. His source data is 14 in his report. He testified to as much. The 15 written report that he submitted as an -- as an 16 expert are the experiments that he says he 17 published. So he is the source and I had that 18 report and I read that report. 19 BY MS. GARBER: 20 Q So his expert report is the totality of 21 his data that was published in the 2019 publication, 22 is that your testimony? 23 A That's his testimony. 24 MS. CURRY: Object to the form. 25 ///</p>	<p style="text-align: right;">Page 108</p> <p>1 MS. GARBER: Sure. I can't give that you 2 to you right now, but you can ask your counsel to 3 look at his report. 4 THE WITNESS: Okay. For the purposes of 5 accuracy, I'd rather not hypothesize about what he 6 had in his report, but if I have it in front of me, 7 I would be happy to comment on it. 8 MS. GARBER: Okay. 9 BY MS. GARBER: 10 Q Where do you list in your references 11 Dr. Saed's abstracts? 12 A I don't recall the name of the first 13 author on anything other than the Fletcher abstract 14 so I don't know where to find it right now. I do 15 believe that I have seen them, but I don't know 16 where it is right now. 17 Q Is it fair to say, Dr. Saenz, that 18 Dr. Saed's abstracts are not listed on any of your 19 reference materials? 20 MS. CURRY: Object to the form. 21 THE WITNESS: I don't think that would be 22 fair to say, because I just am saying that I can't 23 recall who else were first authors on his papers 24 right now. And so I can't be sure that they are 25 aren't actually here, other than the Fletcher paper,</p>
<p style="text-align: right;">Page 107</p> <p>1 BY MS. GARBER: 2 Q And all one needs to do is to read his 3 deposition to fully understand the data that is 4 referenced and described in the 2019 publication, is 5 that your testimony? 6 MS. CURRY: Object to the form. 7 THE WITNESS: You're misstating my 8 testimony. What I said -- 9 BY MS. GARBER: 10 Q Why don't you clarify? 11 A I'd be happy to. What I said is I read 12 his report and his report is the experiments that he 13 did, that he then says he published in his 14 deposition. But the report contains the 15 experiments. He said he did that report for the 16 purposes of evaluating talc and its potential to be 17 carcinogenic, but he states it himself, he is the 18 source. 19 Q Can you tell me from reading his expert 20 report what his methodologies and materials were 21 with regard to his study that was published in 2019? 22 MS. CURRY: Object to the form. 23 THE WITNESS: Can I have his expert 24 report in front of me so that I can make sure I 25 don't misquote anything?</p>	<p style="text-align: right;">Page 109</p> <p>1 or the Fletcher abstract, I should say. But without 2 recalling who the first author was, I just can't 3 recall. 4 BY MS. GARBER: 5 Q You did read Health Canada's draft 6 screening; correct? 7 A Yes. 8 Q Have you read any comment letters or 9 reports issued in response to the Health Canada's 10 December DSAR? 11 MS. CURRY: Object to the form. 12 THE WITNESS: No, I don't believe that I 13 have. 14 BY MS. GARBER: 15 Q Have you or are you planning to comment 16 to Health Canada regarding their assessment? 17 A No, I am not. 18 Q Have you been asked to reply? 19 A No, I have not. 20 Q Have you been asked to testify at any 21 United States or state government proceedings 22 regarding talcum powder products? 23 A No, I have not. 24 Q Are you conducting any research in any 25 capacity concerning talcum powder products and risk</p>

<p style="text-align: right;">Page 110</p> <p>1 of ovarian cancer, and by that I mean in your 2 laboratory or at your institution? 3 A No, ma'am. 4 Q Have you ever applied for a grant or any 5 monies to conduct a research project on talcum 6 powder products and ovarian cancer? 7 A No. 8 Q Do you sit on any editorial boards for 9 any scientific journals? 10 A As a regular editorial board position, 11 no. But I have been an ad hoc reviewer. 12 Q I saw that in your CV. As an ad hoc 13 reviewer, which journals have you served on? 14 A Let me turn to my -- is that my CV? Yes. 15 So I've an ad hoc reviewer for Gynecologic Oncology, 16 for the Gray Journal, which is the American Journal 17 of Obstetrics and Gynecology, for Cancer, and for 18 the Journal of Pediatric Surgery Case Reports. 19 Q In that regard, have you ever reviewed 20 any articles in connection with talcum powder 21 products and risk of ovarian cancer? 22 A No. 23 Q Turning back to your expert report and 24 going through it, there is at the back of your 25 report, a document titled "Table one, analysis of</p>	<p style="text-align: right;">Page 112</p> <p>1 THE WITNESS: I believe that these 2 discrepancies misrepresent the data, and so for the 3 sakeness [sic] of trying to be accurate with the 4 data, I wanted to make sure I had an accurate 5 representation. I do believe that this was in part 6 part of her opinion, otherwise, I don't think she 7 would have put it in her report. 8 BY MS. GARBER: 9 Q Do you have any basis to conclude that 10 she intentionally misrepresented the data? 11 MS. CURRY: Object to the form. 12 THE WITNESS: I don't know why she 13 misrepresented the data. I only know that she did. 14 BY MS. GARBER: 15 Q You read her deposition; did you not? 16 A Yes, I did. 17 Q Did you read both volumes? 18 A Yes, I did. 19 Q What was your understanding of her 20 testimony with regard to table four in her second 21 deposition? 22 A I don't believe I recall specifically 23 getting asked questions about table four in her 24 deposition. I -- 25 Q You didn't read her deposition, did you,</p>
<p style="text-align: right;">Page 111</p> <p>1 case control studies cited by Dr. Smith-Bindman," 2 and table four of her expert report. 3 Do you see that? 4 A Yes. 5 Q What is the nature of that document? 6 A The nature of this document was to 7 analyze and review the case control studies that are 8 cited by Dr. Smith-Bindman in her report as 9 influencing her opinion. But in my review, in 10 reading her report, it became obvious to me that she 11 was mis-transcribing or misquoting the numbers and 12 the odds ratios and the confidence interval from the 13 original documents into her report. 14 So in my review, I wanted to make sure I 15 had accurate data and I found a number of 16 discrepancies. 17 Q Is it your opinion that those 18 discrepancies, as you say, were made intentionally? 19 MS. CURRY: Object to the form. 20 THE WITNESS: I have no idea. 21 BY MS. GARBER: 22 Q Is it your opinion that those 23 discrepancies made a difference in the outcome of 24 her opinions? 25 MS. CURRY: Object to the form.</p>	<p style="text-align: right;">Page 113</p> <p>1 Doctor? 2 A No, that's not true, ma'am. I did read 3 her deposition, both volumes, cover to cover. What 4 I recall the main focus of her deposition testimony 5 was on the individual analysis that she did, which 6 she called her own systematic review of the 7 literature that has been published and the different 8 conditions on which she made that analysis. 9 Q I notice, Doctor, that your chart, which 10 is table one, of her table, table four, you have 11 indicated on the right-hand column mistakes in 12 reported -- mistakes in reported data in table four 13 of Smith-Bindman's report. 14 Is that correct? 15 A Yes. 16 Q Then you go down for the various studies 17 and you indicate a number. So we'll just do for 18 instance, the Schildkraut paper? 19 A Okay. 20 Q You indicate, Schildkraut paper, and you 21 give an odds ratio or a relative risk and then you 22 give a confidence interval; correct? 23 A Well -- 24 MS. CURRY: Object to the form. 25 THE WITNESS: I don't give that. That's</p>

<p style="text-align: right;">Page 114</p> <p>1 what the Schildkraut paper found. 2 BY MS. GARBER: 3 Q That's what I'm trying to understand. So 4 you -- so I understand the nature of your table, 5 you're giving Schildkraut's odds ratio or relative 6 risk for every use of genital talc, and then if we 7 move to the right, you're indicating whether or not 8 it's statistically significant or not statistically 9 significant; correct? 10 A Again, I don't give these. This is the 11 data as reported in the table. 12 Q Understood. 13 A I am generating this table, extracting 14 the data from the report as published, and comparing 15 it to what Dr. Smith-Bindman listed in her table 16 four. 17 So for ever versus never genital-only use 18 of talcum powder products, that's what Schildkraut 19 reports, and Schildkraut reported that that was a 20 statistically significant finding. 21 Q In the next column for the mistakes, what 22 you're indicating here is that Dr. Smith-Bindman 23 reported an incorrect odds ratio in her table four? 24 A That's correct. 25 Q Okay. Now I understand the nature of</p>	<p style="text-align: right;">Page 116</p> <p>1 nature of the table four; correct? 2 A Hold on one second, please. 3 MS. CURRY: Object to the form. 4 THE WITNESS: She's describing that in 5 table four and table four is labeled, "list of 6 included studies with number of cancers, controls 7 and reported odds ratios." So that's the odds ratio 8 that she claims was reported in the study for ever 9 versus never use of perineal -- the perineal 10 application of talc. 11 BY MS. GARBER: 12 Q Does it say that, Doctor? 13 A It does in the title. 14 Q Did she provide any testimony about why 15 those odds ratios are slightly off in her table 16 four? 17 MS. CURRY: Object to the form. 18 THE WITNESS: I don't recall, but I'd be 19 happy to look at the deposition. But specifically 20 with respect to table four, I don't recall. 21 MS. GARBER: Okay. 22 THE WITNESS: I do recall that her own 23 analysis, she changed numbers and things, but this 24 is table four, which is titled "reported odds 25 ratio."</p>
<p style="text-align: right;">Page 115</p> <p>1 your table. 2 A Okay. 3 MS. GARBER: Let's mark 4 Dr. Smith-Bindman's table four and a couple 5 documents that sort of explain it from her report. 6 We'll mark that as Exhibit 6. 7 (C. Saenz Exhibit 6 was marked for 8 identification.) 9 BY MS. GARBER: 10 Q And I'll represent for the record, this 11 does not include every page of her expert report. 12 It's meant to demonstrate table four. And so if you 13 see at the bottom of 18, it starts to describe what 14 is going to be referenced at her table four. 15 Do you see that? 16 A Where are you, ma'am? 17 Q If you go to the top of page 19, first 18 paragraph. It ends -- the last sentence says, "the 19 number of individual women included in each study 20 and the reported or estimated effect size for any 21 exposure to talc adjusted for other risk factors 22 such as age are in table four." 23 Did I read that correctly? 24 A Yes. 25 Q And so there she's just describing the</p>	<p style="text-align: right;">Page 117</p> <p>1 BY MS. GARBER: 2 Q Is the gist of this table that you're 3 trying to convey she's misrepresenting the data, or 4 rather, there's mistakes and she's sloppy, or both? 5 MS. CURRY: Object to the form. 6 THE WITNESS: Again, as I testified 7 earlier, I don't know what her intention was and why 8 the data that is listed as reported odds ratios, 9 which means the published odds ratios, I don't know 10 why in this table it's different than what actually 11 was in the study. I just know that it is. 12 BY MS. GARBER: 13 Q Is it important to get it right in your 14 opinion? 15 MS. CURRY: Object to the form. 16 THE WITNESS: It's important that she -- 17 if she's going to label this as reported odds ratio, 18 it's important that she transcribe the data 19 accurately. 20 BY MS. GARBER: 21 Q Let's look at your table one. Let's look 22 at the Schildkraut study. You stated here that the 23 accurate odds ratio is 1.44 with a confidence 24 interval of 1.11 to 1.86; correct? 25 MS. CURRY: Object to the form.</p>

<p style="text-align: right;">Page 118</p> <p>1 THE WITNESS: For ever versus never</p> <p>2 genital use.</p> <p>3 BY MS. GARBER:</p> <p>4 Q That's incorrect, isn't it?</p> <p>5 A No, it's correct.</p> <p>6 MS. GARBER: I'll mark the Schildkraut</p> <p>7 paper, which is Exhibit 7.</p> <p>8 (C. Saenz Exhibit 7 was marked for</p> <p>9 identification.)</p> <p>10 BY MS. GARBER:</p> <p>11 Q Doctor, in the Schildkraut paper, the</p> <p>12 ever or any genital use, the odds ratio is reported</p> <p>13 a 1.71 with a confidence interval of 1.26 to 2.33;</p> <p>14 correct?</p> <p>15 A Where are you, ma'am?</p> <p>16 Q I'm at page 1413.</p> <p>17 A And where?</p> <p>18 Q Under the results, at the bottom of the</p> <p>19 page.</p> <p>20 Doctor, is that what it says?</p> <p>21 A That's --</p> <p>22 MS. CURRY: Object to the form.</p> <p>23 THE WITNESS: -- what you're reading,</p> <p>24 however --</p> <p>25 ///</p>	<p style="text-align: right;">Page 120</p> <p>1 Q Doctor, doesn't the ever use under table</p> <p>2 two give the odds ratio of 1.39 with a confidence</p> <p>3 interval of 1.10 to 1.76?</p> <p>4 MS. CURRY: Object to the form.</p> <p>5 THE WITNESS: That's for body powder</p> <p>6 uses, ma'am. That's not restricted to genital use.</p> <p>7 BY MS. GARBER:</p> <p>8 Q Okay, Doctor. Let's turn to</p> <p>9 Dr. Smith-Bindman's deposition testimony.</p> <p>10 MS. CURRY: We've gone an hour, so if you</p> <p>11 need a break, just let us know.</p> <p>12 THE WITNESS: Okay.</p> <p>13 BY MS. GARBER:</p> <p>14 Q Do you have any recollection of what she</p> <p>15 said, why those numbers were slightly off on table</p> <p>16 four in her deposition?</p> <p>17 A No, ma'am, I already testified I'd need</p> <p>18 to look at her deposition to testify specifically.</p> <p>19 Do you have a copy of her deposition</p> <p>20 testimony?</p> <p>21 Q I do.</p> <p>22 A Thank you.</p> <p>23 ///</p> <p>24 ///</p> <p>25 ///</p>
<p style="text-align: right;">Page 119</p> <p>1 BY MS. GARBER:</p> <p>2 Q Doctor, is that what it says?</p> <p>3 A Ma'am, ma'am, I said that's what you're</p> <p>4 reading. But I need you to turn to the next page,</p> <p>5 which is table two, which shows any genital use has</p> <p>6 an odds ratio of 1.44 with a confidence interval of</p> <p>7 1.11 on to 1.86, which is the ever versus never use.</p> <p>8 And that is where I draw my figure from.</p> <p>9 Q Doctor, you drew your figure from the</p> <p>10 abstract, didn't you?</p> <p>11 A No.</p> <p>12 MS. CURRY: Object to the form.</p> <p>13 THE WITNESS: I drew my figure from this</p> <p>14 table.</p> <p>15 BY MS. GARBER:</p> <p>16 Q And though you didn't report under the</p> <p>17 result section any genital powder use odds ratio</p> <p>18 1.71?</p> <p>19 A Because that has to do with daily use.</p> <p>20 That's not any use ever. Any use ever is what's in</p> <p>21 table two. The table four, as in the Smith-Bindman</p> <p>22 study, didn't qualify that it was for any daily use.</p> <p>23 What you're reading from is any daily</p> <p>24 use, whereas table two is an ever versus never,</p> <p>25 which doesn't qualify the dosing to be daily.</p>	<p style="text-align: right;">Page 121</p> <p>1 MS. GARBER: I'll represent for the</p> <p>2 record that this is not her complete deposition, but</p> <p>3 an excerpt where she testified about this topic.</p> <p>4 (C. Saenz Exhibit 8 was marked for</p> <p>5 identification.)</p> <p>6 BY MS. GARBER:</p> <p>7 Q Doctor, this deposition was on Friday,</p> <p>8 February 8th, on 2019; correct, Volume two?</p> <p>9 A That's what it says.</p> <p>10 Q And that is reflected that you read this</p> <p>11 deposition on your reference list; correct?</p> <p>12 A Yes, ma'am.</p> <p>13 Q If we turn to page 254 of her deposition.</p> <p>14 A Okay.</p> <p>15 Q She was asked, was she not, what she did</p> <p>16 to prepare for the deposition since yesterday, and</p> <p>17 at lines 13 through 17, does she indicate that she</p> <p>18 called the biostatistician who worked on the</p> <p>19 meta-analysis for review for a few details, and that</p> <p>20 her name was Dr. Hall?</p> <p>21 A That's what it says.</p> <p>22 Q Do you understand from reading her</p> <p>23 deposition that it was Dr. Hall, the</p> <p>24 biostatistician, who ran these numbers and not</p> <p>25 Dr. Bindman?</p>

<p style="text-align: right;">Page 122</p> <p>1 A That's what I understand from the 2 deposition testimony. 3 Q And then if you turn to page 255, at 4 lines 16 through 25, it indicates what notes did you 5 make from your conversation with Dr. Hall. And she 6 explains that she mostly asked her to clarify about 7 how she did the calculations and the numbers that 8 are shown in the figures. 9 She goes on to explain, she was 10 struggling to see why they were not exactly the same 11 as the ones shown in the published studies. 12 And then it -- 13 A Ma'am, I'm sorry, I believe you're 14 misquoting what it says here. 15 Q Okay. What do you think it says? 16 A It says, "I was struggling to understand 17 why the numbers and the figures were not exactly the 18 same as the ones that you showed me in the published 19 manuscript." So that's not the same as saying, in 20 published studies. 21 What Dr. Smith-Bindman is testifying to 22 here is what I was referencing before. These are 23 questions about her own meta-analysis. These are 24 not questions that are referring to table four. 25 Table four is separate and distinct from</p>	<p style="text-align: right;">Page 124</p> <p>1 not necessarily a problem with the software. She 2 specified that the calculations were made by the 3 software in the program she used. But there's 4 absolutely no reference here specifically to table 5 four. 6 Q Do you harbor the opinion that 7 Dr. Smith-Bindman intentionally misrepresented her 8 numbers? 9 MS. CURRY: Object to the form. 10 THE WITNESS: I harbor the opinion that 11 table four in Dr. Smith-Bindman's report, which is 12 listed as the transcription of the reported odds 13 ratios from the published literature as ever versus 14 never use, are not actually the numbers that were in 15 that publication, or those publications. That is 16 different than her own meta-analysis, which was her 17 own analysis that she did at the end of her report. 18 I don't know what her motivation was. Do 19 I know that the numbers that she reported are wrong, 20 where I have highlighted that they're wrong. 21 BY MS. GARBER: 22 Q And if in fact, it's her testimony that 23 those number are slightly off and she was not aware 24 they were slightly off, but it was attributable to 25 her biostatistician's application of a software</p>
<p style="text-align: right;">Page 123</p> <p>1 her own meta-analysis. So all of this conversation 2 in her deposition is with regards to the 3 meta-analysis that she did separate and apart from 4 table four. 5 Q That's your understanding of her 6 testimony? 7 A That is -- 8 MS. CURRY: Object to the form. 9 THE WITNESS: That is what is there. 10 BY MS. GARBER: 11 Q Let's go on to page 257. On page 257, 12 lines one through nine, does she explain that the 13 discrepancies between the studies and what was 14 reported on table four was attributable to issues 15 with the software that the biostatistician used in 16 running those numbers? 17 MS. CURRY: Object to the form. 18 THE WITNESS: I'll need to read this, 19 ma'am. 20 BY MS. GARBER: 21 Q Okay. 22 A She makes absolutely no specific 23 reference to table four. She talks about that there 24 are some numbers that she didn't understand, that 25 the statistician then says that there were -- it was</p>	<p style="text-align: right;">Page 125</p> <p>1 program, do you have any criticisms of her table 2 four? 3 MS. CURRY: Object to the form. 4 THE WITNESS: Yes, I do. This is not a 5 calculation. This is a reporting of the data from 6 the studies that were published. Whatever software 7 program her statistician used had nothing to do with 8 the production of the numbers that are in table 9 four. The software program that she used was for 10 the purposes of her own meta-analysis. 11 Table four is supposed to be where she 12 looked at the published literature and transcribed 13 the number. There were no computations that were 14 supposed to be getting done in table four as she 15 reported table four. 16 BY MS. GARBER: 17 Q Do you have any basis to conclude that 18 those slight deviations from what was in the 19 published literature affected her opinions in any 20 way? 21 MS. CURRY: Object to the form. 22 THE WITNESS: Yes, I do. Because she 23 reported odds ratios that were incorrect and were 24 inflated from what was actually published in the 25 literature.</p>

<p style="text-align: right;">Page 126</p> <p>1 BY MS. GARBER:</p> <p>2 Q Were they all inflated?</p> <p>3 A No, and I didn't say they were all</p> <p>4 inflated. I listed when there were no mistakes in</p> <p>5 what she transcribed.</p> <p>6 Q And were there were mistakes, were those</p> <p>7 always an inflation of the data or were they</p> <p>8 sometimes a deflation of data?</p> <p>9 A I can't recall the exact nature of all of</p> <p>10 them, ma'am. There's something like 30 studies</p> <p>11 here.</p> <p>12 Q Wouldn't that make a difference,</p> <p>13 Dr. Saenz? If she had deflated the value, that</p> <p>14 wouldn't have affected her opinion, would it?</p> <p>15 MS. CURRY: Object to the form.</p> <p>16 BY MS. GARBER:</p> <p>17 Q Doesn't it show that this was not done</p> <p>18 intentionally?</p> <p>19 A I don't think it -- we have any idea</p> <p>20 whatsoever what her intent was. The data was wrong.</p> <p>21 And when you're producing a report such as this and</p> <p>22 you say that this is the data that's reported in</p> <p>23 those studies, then you have a responsibility to</p> <p>24 accurately report that data.</p> <p>25 The directionality of it doesn't make it</p>	<p style="text-align: right;">Page 128</p> <p>1 We're going off the record.</p> <p>2 (Lunch break taken at 12:00 p m.)</p> <p>3 0o0</p> <p>4 (The deposition resumed at 12:59 p.m.)</p> <p>5 0o0</p> <p>6 THE VIDEOGRAPHER: The time is now 12:58.</p> <p>7 Back on the record.</p> <p>8 BY MS. GARBER:</p> <p>9 Q Good afternoon, Dr. Saenz.</p> <p>10 A Good afternoon.</p> <p>11 Q With regard to Exhibit 5, your expert</p> <p>12 report, your CV is attached to the back of it; is</p> <p>13 that right?</p> <p>14 A Yes.</p> <p>15 Q And it looks like it was last updated</p> <p>16 February of 2019; is that right?</p> <p>17 A Correct.</p> <p>18 Q Are there any amendments that you need to</p> <p>19 make to your CV to make it accurate?</p> <p>20 A No.</p> <p>21 Q Does it accurately reflect all your</p> <p>22 publications?</p> <p>23 A Yes.</p> <p>24 Q You don't hold yourself out as a cancer</p> <p>25 biologist, do you?</p>
<p style="text-align: right;">Page 127</p> <p>1 right or -- it's wrong to incorrectly report the</p> <p>2 data.</p> <p>3 Q In reading her deposition, did you glean</p> <p>4 from that that she realized that those data were</p> <p>5 misreported and she tried to explain why they were</p> <p>6 misreported?</p> <p>7 MS. CURRY: Object to the form.</p> <p>8 THE WITNESS: Again, the deposition</p> <p>9 testimony that you're handing me here is an</p> <p>10 explanation of what her meta-analysis was and the</p> <p>11 software programming that was used in order to</p> <p>12 conduct her meta-analysis, it has nothing to do with</p> <p>13 what's been produced in table four.</p> <p>14 MS. GARBER: That's your opinion.</p> <p>15 MS. CURRY: Object to the form.</p> <p>16 THE WITNESS: That's documented in her</p> <p>17 report and in the testimony she gave. She talks</p> <p>18 about this being for her meta-analysis, not for</p> <p>19 table four.</p> <p>20 MS. GARBER: Let's turn back to your</p> <p>21 expert report.</p> <p>22 THE WITNESS: Can we take a break?</p> <p>23 MS. GARBER: Yes. It's a good breaking</p> <p>24 point.</p> <p>25 THE VIDEOGRAPHER: The time is 11:59.</p>	<p style="text-align: right;">Page 129</p> <p>1 MS. CURRY: Object to the form.</p> <p>2 THE WITNESS: I'm not formally trained in</p> <p>3 cancer biology, but I have certainly worked in</p> <p>4 cancer biology labs and I read the cancer biology</p> <p>5 literature as it pertains to gynecologic</p> <p>6 malignancies.</p> <p>7 BY MS. GARBER:</p> <p>8 Q You don't have any degrees in</p> <p>9 epidemiology?</p> <p>10 A I do not have any degrees in</p> <p>11 epidemiology.</p> <p>12 Q You don't hold yourself out as an</p> <p>13 epidemiologist, do you?</p> <p>14 A I'm not formally trained in epidemiology,</p> <p>15 but I've published epidemiologic literature and I</p> <p>16 certainly review epidemiologic literature on a</p> <p>17 regular basis as pertains to gynecologic oncology.</p> <p>18 MS. GARBER: Motion to strike as</p> <p>19 nonresponsive.</p> <p>20 BY MS. GARBER:</p> <p>21 Q Doctor, my question was, do you hold</p> <p>22 yourself out as an epidemiologist?</p> <p>23 A I do have expertise in epidemiology and</p> <p>24 gynecologic oncology.</p> <p>25 Q Do you hold yourself out as an</p>

Page 130

1 epidemiologist? If I go to your website, does it
 2 say you're an epidemiologist?
 3 A I don't have a website.
 4 Q If I went to a bio about you, does it say
 5 you're a epidemiologist?
 6 A It says I'm an expert in gynecologic
 7 oncology and in that includes literature on the
 8 epidemiology of gynecologic oncology.
 9 Q How many times have you served as an
 10 ad hoc reviewer?
 11 A Upwards of 20.
 12 Q When was the last time you served as an
 13 ad hoc reviewer?
 14 A Approximately two months ago.
 15 Q What journal?
 16 A Gynecologic Oncology.
 17 Q Were any of the papers that you reviewed
 18 regarding ovarian cancer?
 19 A Over the course of my career?
 20 Q I'm sorry, were any of the papers that
 21 you reviewed as an ad hoc reviewer, did the topic
 22 concern ovarian cancer?
 23 A Right. So for clarification purposes,
 24 you mean over the course of my career?
 25 Q Yes.

Page 131

1 A Yes.
 2 Q When was the last time?
 3 A Oh, I don't remember. I review somewhere
 4 around two to three articles a year.
 5 Q Do you know the -- based on you being an
 6 ad hoc reviewer for gynecologic -- well, strike
 7 that.
 8 Have you reviewed abstracts for the
 9 Society for Gynecologic Oncology?
 10 A Yes.
 11 Q When is the last time you did that?
 12 A You mean for the annual meeting itself?
 13 Q Yes.
 14 A I would say, two to three years ago.
 15 Q How many times have you done that kind of
 16 work in general?
 17 A At least three.
 18 Q In that regard, did you ever review any
 19 papers on the topic of ovarian cancer?
 20 A Yes.
 21 Q In that regard, did you review papers or
 22 presentations on the topic of talc and ovarian
 23 cancer?
 24 A No.
 25 Q Attendant to your work as an ad hoc

Page 132

1 reviewer for SGO, do you know what their policies
 2 and procedures are for review and acceptance?
 3 MS. CURRY: Object to the form.
 4 THE WITNESS: So I think you're kind of
 5 mixing apples and oranges. When you review for the
 6 annual meeting for SGO, you're not an ad hoc
 7 reviewer. You're somebody that's either volunteered
 8 to review the abstracts for presentation at the
 9 meeting, or you're on the program committee and it's
 10 your responsibility to review those abstracts.
 11 Or you're on the marketing and
 12 communications committee and you're asked to do it
 13 in that role as well.
 14 BY MS. GARBER:
 15 Q And in the three times that you have
 16 served as a reviewer, what was your role for SGO?
 17 A So two of the times, I was invited to
 18 review abstracts and to score them. And one of the
 19 times, I was actually a member of the program
 20 committee that year.
 21 Q The two times that you were invited to
 22 review and score, what were -- what was the nature
 23 of the articles you were reviewing?
 24 A It was the breath and depth of
 25 gynecologic oncology because I reviewed over 300

Page 133

1 abstracts for the annual meeting on each of those
 2 occasion.
 3 Q But none of those involved talcum ovarian
 4 cancer?
 5 A Not that I recall.
 6 Q The one additional time, what was the
 7 nature of that one?
 8 A I was on the program committee.
 9 Q What does that entail?
 10 A That entails reviewing all of abstracts,
 11 scoring them, and then going to a venue, if you
 12 will, almost a two to three-day retreat where the
 13 people that are actually on the program committee
 14 decide which abstracts are being accepted, which
 15 will be posters, which will be oral presentations,
 16 and which will be highlighted with reference to
 17 invited speakers.
 18 Q Would you say based on your experience,
 19 it's a rigorous review to be accepted to present at
 20 SGO?
 21 MS. CURRY: Object to the form.
 22 THE WITNESS: In what capacity?
 23 BY MS. GARBER:
 24 Q Scientific capacity.
 25 MS. CURRY: Object to the form.

Page 134

1 THE WITNESS: So I think that's really
 2 kind of a gross overgeneralization of the way that
 3 the meeting occurs. There are different levels of a
 4 claim, if you will, or scientific accord of the
 5 abstracts, based on whether or not you're accepted
 6 for a plenary session presentation versus a breakout
 7 session versus a poster session.
 8 And so the scientific acclaim with each
 9 of those is really in descending order.
 10 BY MS. GARBER:
 11 Q Are you familiar with, I'll use the
 12 phrase, policies and procedures or sort of the
 13 context in which you would review data for the SGO?
 14 MS. CURRY: Object to the form.
 15 THE WITNESS: What do you mean by "data"?
 16 BY MS. GARBER:
 17 Q In other words, the review process, say
 18 were you asked to review and you were invited to
 19 review and to score data or a presentation. Are you
 20 familiar with policies and procedures of how that's
 21 done generally speaking?
 22 A Well --
 23 Q In other words, is it five people, is it
 24 ten people? What level of review is it? Just give
 25 me a feel for how that process happens.

Page 135

1 MS. CURRY: Object to the form.
 2 THE WITNESS: So I'm only familiar with
 3 respect to the three times that I did serve as a
 4 review for the meeting. So to that extent, yes.
 5 BY MS. GARBER:
 6 Q To that extent, yes, what?
 7 A During the three times that I did serve
 8 as a reviewer for the annual meeting, I'm familiar
 9 with the policies and procedures.
 10 Q Okay. And what are these?
 11 MS. CURRY: Object to the form.
 12 THE WITNESS: I don't know what the
 13 current ones are, but because I'm not on the program
 14 committee this year. But when I did serve, there
 15 can be many dozen of people that review abstracts,
 16 but then the ultimate decision amongst the program
 17 committee as to what makes it to plenary sessions
 18 versus breakout sessions versus a poster is decided
 19 by a committee of -- I believe our program committee
 20 was around 20 people.
 21 BY MS. GARBER:
 22 Q Are you planning to go to SGO this year?
 23 A I was.
 24 Q What did you do to prepare for today's
 25 deposition?

Page 136

1 A Other than write the report? I, as we
 2 discussed earlier, read the Penninkilampi article
 3 again last evening. I looked up some other articles
 4 on COX and ovarian cancer. I've read my own report.
 5 I met with counsel in preparation for
 6 today. And generally read all the expert reports
 7 that we talked about, read the depositions that are
 8 listed in my reference, and re-reviewed the
 9 literature that is in my report over a long time
 10 period.
 11 Q In preparation for today's deposition,
 12 how many meetings did you have with counsel?
 13 A Since what time period?
 14 Q Just in preparation for today's
 15 deposition as you would understand that question.
 16 A Do we mean back to when I was first
 17 retained for this matter or do we mean since my
 18 report was submitted?
 19 Q In connection with preparing for today's
 20 deposition, did you meet with counsel?
 21 A Specifically for today's deposition, I've
 22 had one meeting.
 23 Q How long was that meeting?
 24 A About two and a half hours.
 25 Q Who was present?

Page 137

1 A Ms. Curry.
 2 Q Anybody else?
 3 A No.
 4 Q Were any lawyers on the phone?
 5 A No. I was there too obviously.
 6 Q Did you have any other meetings with
 7 Ms. Curry or any other lawyers in connection with
 8 today's deposition, preparing for it specifically?
 9 A No.
 10 Q With regard to the documents that you
 11 reviewed that you've told us about, how many hours
 12 would you say you've reviewed those?
 13 A Probably in sum total, somewhere around
 14 75 to 80 hours.
 15 Q So between, I thought you said between
 16 February of '19 and today, you had worked about
 17 15 hours?
 18 A Correct.
 19 Q So how many hours did it take you to
 20 review the documents that you reference? The
 21 Penninkilampi and the COX-2 and to re-review your
 22 report and those types of things, how many hours did
 23 that take?
 24 A About two hours.
 25 Q Other than counsel, have you told me

<p style="text-align: right;">Page 138</p> <p>1 about all conversations that you've had concerning 2 this matter? I think it's none, but there aren't 3 any other people other than counsel you've discussed 4 this case with; is that a true statement? 5 A That's a true statement. 6 Q I was asking you about internal documents 7 earlier, and I want to be sure I understand some of 8 your answers. 9 Do you harbor any opinions about whether 10 or not internal documents are reliable for forming 11 the basis of an expert opinion? 12 MS. CURRY: Object to the form. 13 THE WITNESS: I have no opinion on that. 14 I don't believe it's -- I don't believe it's 15 important to generating my opinion. I believe that 16 my opinion is based on what we discussed before. So 17 internal documents don't influence my opinion one 18 way or another. 19 BY MS. GARBER: 20 Q So if you saw a document wherein Johnson 21 & Johnson employees were admitting -- I'll just 22 throw out a hypothetical -- talc can migrate, 23 there's compelling evidence that talc can migrate, 24 that wouldn't influence your opinion? 25 MS. CURRY: Object to the form.</p>	<p style="text-align: right;">Page 140</p> <p>1 MS. CURRY: Object to the form. 2 THE WITNESS: No. 3 BY MS. GARBER: 4 Q Are you aware of that? 5 A No. 6 Q Do I now have the full list of the 7 documents that you considered in formulating your 8 opinions as referenced in your February 2019 report? 9 MS. CURRY: Object to the form. 10 THE WITNESS: So I think there may be 11 some confusion with respect to the Saed abstract 12 that's in my report versus what has been presented 13 in -- I should say in a published format as what was 14 the meeting that was accepted at -- I'm sorry, the 15 abstract that was accepted at a meeting, but then 16 later published in the Journal of Reproductive 17 Sciences as the abstract that had been presented at 18 the meeting. 19 During the break, I asked counsel to show 20 me the abstract and there seems to be two abstracts 21 from Fletcher and Saed that have different topics 22 but are from the same meeting. 23 So the confusion for me was that I didn't 24 realize that they were two. One is referencing the 25 CA 125, and I think that's the abstract that was</p>
<p style="text-align: right;">Page 139</p> <p>1 THE WITNESS: I base my opinions on the 2 peer-reviewed literature and there is no literature 3 that supports that preposition [sic]. 4 BY MS. GARBER: 5 Q There's no literature? 6 A Not on the perineum to the ovaries, no. 7 Q Do you limit it to that? 8 A That's the case that we're discussing, 9 that's my review. 10 Q So when you say there's no literature 11 that supports talc can migrate, you're limiting that 12 body of literature from the perineum to the vagina; 13 is that true? 14 MS. CURRY: Object to the form. 15 THE WITNESS: No, I'm qualifying my 16 statement that the application of talc from the 17 perineum and whether or not it can migrate to the 18 ovaries, there's no literature that supports that 19 hypothesis. 20 BY MS. GARBER: 21 Q Okay. We'll get to that shortly. 22 Are you aware of circumstances where 23 scientists have gained access to internal company 24 documents and rely upon those in formulating their 25 opinions for scientific publications?</p>	<p style="text-align: right;">Page 141</p> <p>1 listed as to be presented at the meeting in March 2 of 2018, but then the actual journal published a 3 different abstract. 4 So that's wherein the confusion lies. 5 BY MS. GARBER: 6 Q So are you saying now after lunch break 7 and talking to counsel, you need to correct your 8 reference list? 9 MS. CURRY: Object to the form. 10 THE WITNESS: I need -- so the reference 11 is correct in the sense that that is what was 12 published in the Journal of Reproductive Sciences. 13 But the abstract that talks about CA 125 looks to me 14 as though it's from the program and it's not the 15 same abstract as what was then published in the 16 Journal of Reproductive Sciences. 17 So, yes, we likely should add that other 18 abstract that wasn't in the program. 19 BY MS. GARBER: 20 Q So you're now saying we need to add 21 something to your reference list? 22 A Correct. I've seen both of those. It 23 wasn't on my list, but I think that's because one 24 was in the program, the other was in the journal, 25 and they don't match, which means most likely</p>

Page 142

1 additional data was added to what was the program
2 aspect when it finally was published in the journal.
3 Q What is the title of the abstract that
4 you say we now need to add to your reference list?
5 MS. CURRY: I actually have a copy of it
6 if that would be helpful, if you want to mark it as
7 an exhibit.
8 MS. GARBER: Sure.
9 MS. CURRY: I'll give you a copy of both
10 of the abstracts that Dr. Saenz just testified
11 about.
12 (C. Saenz Exhibit 9 was marked for
13 identification.)
14 BY MS. GARBER:
15 Q Doctor, I'm going to mark as Exhibit 9,
16 an abstract that --
17 A If you want to give me the marked one --
18 Q Thank you. That counsel just handed me.
19 The first of two documents that counsel just handed
20 me.
21 A Right.
22 Q The first is dated March 10th, 2018, and
23 it's from SRI, 65th annual scientific meeting, and
24 it's titled "Talcum powder enhances cancer antigen
25 125 levels in ovarian cancer cells and in normal

Page 143

1 ovarian epithelial cells."
2 Doctor, this is the abstract that was
3 originally reflected on your reference as
4 reference 21; is that correct?
5 MS. CURRY: Object to the form.
6 THE WITNESS: I don't actually think
7 that's correct, ma'am. I think that the second one
8 is actually the one that's listed in my reference
9 list as number 21.
10 This one, Exhibit 9, is the abstract that
11 I believe comes from the program that was to be --
12 that was for the meeting, the 65th annual meeting of
13 SRI, which was on March 10th.
14 But then when the program abstracts were
15 published, the abstract was modified. And that's
16 what ends up in the journal and is my reference 21.
17 MS. GARBER: Okay.
18 THE WITNESS: But I've seen both of
19 these, and that's where my confusion lied, because
20 they're both from the same meeting. It's just that
21 the one that was published in the journal was
22 modified from the one that was published in the
23 meeting program.
24 BY MS. GARBER:
25 Q Doctor, you didn't type yourself, did

Page 144

1 you, pages 32 through 42, of your expert report, did
2 you?
3 A I supplied the reference to counsel, but
4 I did not format this list, that's correct.
5 Q Do you have a folder on your computer
6 which reflects the body of literature that you have
7 reviewed in connection with your expert opinions
8 that formulate the reference that you have provided
9 us?
10 A Yes.
11 MS. CURRY: Object to the form.
12 BY MS. GARBER:
13 Q You have not brought with you that body
14 of literature with you today.
15 A It's all on my computer, ma'am.
16 Q It can be downloaded to a jump drive;
17 right?
18 A Potentially, yes.
19 MS. GARBER: Let's mark as Exhibit 10 a
20 document.
21 (C. Saenz Exhibit 10 was marked for
22 identification.)
23 BY MS. GARBER:
24 Q And, Doctor, this would reflect an
25 abstract titled "F-098, talcum powder enhances

Page 145

1 oxidative stress in ovarian cancer cells," Nicole
2 Fletcher, Ira Memaj, and Dr. Saed.
3 Is that correct?
4 A That's correct.
5 Q It's your testimony that in connection
6 with your expert report, you had reviewed this
7 abstract?
8 A Yes, ma'am.
9 Q Do you now need to add any other
10 documents to your reference list that we have
11 reviewed today to make it accurate to reflect what
12 you have reviewed in connection with your expert
13 report or expert opinions today?
14 MS. CURRY: Object to the form.
15 THE WITNESS: So with respect to what I
16 have cited in the report, no. Obviously, I've had a
17 very long career and there's literature that I've
18 read that is not in this report or in my reliance
19 list over the course of time, but nothing else that
20 I've referenced to or cited for the purposes of this
21 report, other than my general fount of knowledge.
22 BY MS. GARBER:
23 Q I appreciate that. You understand that
24 I'm entitled to know the literature you considered
25 in formulating your opinions; correct?

<p style="text-align: right;">Page 146</p> <p>1 A Absolutely. Which is why I tried to 2 figure out at lunchtime why there was a discrepancy. 3 Q Do you have any documentation which 4 evidences -- strike that. 5 What was your assignment as you 6 understood it when you were first retained by the 7 MDL lawyers for Johnson & Johnson? 8 MS. CURRY: Object to the form. 9 THE WITNESS: For this particular matter? 10 MS. GARBER: Yes. 11 THE WITNESS: To review the literature on 12 the topic of perineal application of talc and the 13 risk of developing ovarian cancer, to write a report 14 on that, as well as on the same evaluation that 15 plaintiff's experts made, and to essentially get my 16 opinion down on paper. 17 BY MS. GARBER: 18 Q Were you asked to render a causation 19 opinion? 20 MS. CURRY: Object to the form. 21 THE WITNESS: With respect to whether or 22 not talc causes ovarian cancer -- the perineal 23 application of talc causes ovarian cancer, I would 24 say in the broadest sense; yes. 25 ///</p>	<p style="text-align: right;">Page 148</p> <p>1 certainly my hope that we can identify causes of 2 ovarian cancer, but I don't think the science is 3 there right now. 4 BY MS. GARBER: 5 Q So you understood that one of the 6 questions that you were asked to determine is 7 whether talcum powder products can cause ovarian 8 cancer; in other words, a general causation opinion. 9 Generally speaking, can ovarian -- sorry, can talcum 10 powder products cause ovarian cancer? 11 MS. CURRY: Object to the form. 12 THE WITNESS: Right. So in the broad 13 sense of, does -- is hypothesis supported by the 14 epidemiology, the mechanistic studies that exist, 15 the bio -- the migration theory that's been put 16 forth, the patient data, the clinical data that we 17 know and that we see, is the hypothesis that 18 perineal application of talc can cause ovarian 19 cancer, is that substantiated or not. 20 BY MS. GARBER: 21 Q That's a different question. I just want 22 to be sure I know your opinions because I don't 23 think it's clear from your report. 24 Are you going to give an opinion, and is 25 it your opinion, can talcum powder products cause</p>
<p style="text-align: right;">Page 147</p> <p>1 BY MS. GARBER: 2 Q Why do you say in the broadest sense? 3 What do you mean by that? 4 A Well, because I don't believe in any one 5 individual woman that we know what causes ovarian 6 cancer, and the issue that was put forth to me that 7 I was asked to comment on was whether or not the 8 hypothesis that perineal application of talc 9 increased the risk of ovarian cancer made sense from 10 an epidemiologic standpoint, from a biologic 11 plausibility standpoint, from a mechanistic 12 standpoint. So that's what I mean by in the 13 broadest sense. 14 BY MS. GARBER: 15 Q Are you saying that scientists can 16 determine what causes ovarian cancer in women 17 generally, but not what caused a given woman's 18 ovarian cancer? 19 MS. CURRY: Object to the form. 20 THE WITNESS: So I think science is 21 trying to determine in the broadest sense what 22 causes ovarian cancer, but I think the state of the 23 science as it exists right now has only been to 24 identify known associated risk factors. 25 I think that, as time goes on, it's</p>	<p style="text-align: right;">Page 149</p> <p>1 ovarian cancer -- epithelial ovarian cancer, is that 2 your opinion? 3 A My opinion -- 4 MS. CURRY: Object to the form. 5 THE WITNESS: -- is that talcum powder 6 products cannot cause ovarian cancer. 7 BY MS. GARBER: 8 Q Is it your opinion that talcum powder 9 products are a risk factor for epithelial ovarian 10 cancer? 11 A It is my opinion that talcum powder 12 products are not a risk factor for the development 13 of ovarian cancer. 14 Q Is it your opinion that asbestos can 15 cause ovarian cancer? 16 A It -- 17 MS. CURRY: Object to the form. 18 THE WITNESS: It is my opinion that IARC 19 has identified asbestos as causing ovarian cancer in 20 women with heavy occupational exposure, but in the 21 context of whether or not there is asbestos in the 22 talcum powder products, I do not believe that 23 asbestos, nor the talcum powder products themselves, 24 can cause ovarian cancer. 25 ///</p>

<p style="text-align: right;">Page 150</p> <p>1 BY MS. GARBER:</p> <p>2 Q Is it your opinion, Doctor -- I heard all</p> <p>3 that. Is it your opinion that asbestos can cause</p> <p>4 epithelial ovarian cancer?</p> <p>5 MS. CURRY: Object to the form.</p> <p>6 THE WITNESS: Independent of IARC's</p> <p>7 findings?</p> <p>8 BY MS. GARBER:</p> <p>9 Q I didn't ask you that. I just want to</p> <p>10 know what your opinion is. I don't want you to</p> <p>11 qualify it. Just it's a yes-or-no question.</p> <p>12 Can asbestos cause epithelial ovarian</p> <p>13 cancer?</p> <p>14 MS. CURRY: Object to the form, asked and</p> <p>15 answered.</p> <p>16 THE WITNESS: So I don't think I can</p> <p>17 answer it as a yes-or-no question, because I don't</p> <p>18 think the literature is clear on that topic.</p> <p>19 BY MS. GARBER:</p> <p>20 Q Is it your opinion that heavy</p> <p>21 occupational use of asbestos can cause ovarian</p> <p>22 cancer?</p> <p>23 A Same answer. I don't think I can answer</p> <p>24 that as a yes-or-no question because I think the</p> <p>25 literature on that topic is not entirely clear.</p>	<p style="text-align: right;">Page 152</p> <p>1 asbestos increasing the risk of ovarian cancer.</p> <p>2 BY MS. GARBER:</p> <p>3 Q I didn't ask you for a clear role. In</p> <p>4 your opinion, is asbestos a risk factor for</p> <p>5 epithelial ovarian cancer?</p> <p>6 A Again, I don't think that's a yes-or-no</p> <p>7 answer, because I think the literature is somewhat</p> <p>8 inconsistent on that particular topic.</p> <p>9 Q So you don't have that opinion?</p> <p>10 MS. CURRY: Object to the form.</p> <p>11 THE WITNESS: I don't have an opinion</p> <p>12 that it does or that it does not; correct.</p> <p>13 BY MS. GARBER:</p> <p>14 Q You reviewed some of the plaintiff's</p> <p>15 expert purports; correct?</p> <p>16 A That's correct.</p> <p>17 Q Those are all indicated on your reference</p> <p>18 list; correct?</p> <p>19 A Yes.</p> <p>20 Q Would you agree that there are multiple</p> <p>21 epidemiological studies that are cited in those</p> <p>22 reports that showed an association between genital</p> <p>23 use of talcum powder products and ovarian cancer?</p> <p>24 MS. CURRY: Object to the form.</p> <p>25 THE WITNESS: I would agree that some of</p>
<p style="text-align: right;">Page 151</p> <p>1 Q That is inconsistent with your prior</p> <p>2 testimony, isn't it?</p> <p>3 MS. CURRY: Object to the form.</p> <p>4 THE WITNESS: I don't believe that it is.</p> <p>5 MS. GARBER: Okay. We'll get to that.</p> <p>6 BY MS. GARBER:</p> <p>7 Q I think -- I think we already identified,</p> <p>8 but just let me be sure. You do not have any</p> <p>9 opinions as to whether heavy metals can cause</p> <p>10 epithelial ovarian cancer; is that true?</p> <p>11 A So I have not reviewed the literature on</p> <p>12 heavy metals in ovarian cancer, so you are correct.</p> <p>13 I'm not giving an opinion on that.</p> <p>14 Q You are not giving an opinion on whether</p> <p>15 fragrance can cause epithelial ovarian cancer?</p> <p>16 A Likewise, I'm not giving an opinion on</p> <p>17 that.</p> <p>18 Q Is asbestos a risk factor for epithelial</p> <p>19 ovarian cancer?</p> <p>20 MS. CURRY: Object to the form.</p> <p>21 THE WITNESS: So again, based on my</p> <p>22 review of the IARC 2012 document, and based on the</p> <p>23 literature that I reviewed, including the Langseth</p> <p>24 paper, I do not believe that the literature that's</p> <p>25 been published to date supports a clear role for</p>	<p style="text-align: right;">Page 153</p> <p>1 the experts' reports cite to different epidemiologic</p> <p>2 literature. Some of that is demonstrating a weak</p> <p>3 association with the use of perineal talc in the</p> <p>4 development of ovarian cancer, in particular, in the</p> <p>5 case control studies, but there's also other</p> <p>6 literature that does not demonstrate such an</p> <p>7 association.</p> <p>8 BY MS. GARBER:</p> <p>9 Q How do you define weak, as you used it?</p> <p>10 A Weak would be an odds ratio of less than</p> <p>11 two. For this literature in particular, the odds</p> <p>12 ratio tends to be in the range of 1.2 to 1.4.</p> <p>13 Q Are you saying a weak odds ratio is</p> <p>14 anything less than 2.0, the point estimate?</p> <p>15 MS. CURRY: Object to the form.</p> <p>16 THE WITNESS: I'm saying that the odds</p> <p>17 ratios that have been shown in the literature on the</p> <p>18 case control studies are in the range of 1.2 to 1.4.</p> <p>19 It's not a strong association.</p> <p>20 BY MS. GARBER:</p> <p>21 Q I'm trying to get your definition of what</p> <p>22 you mean by weak association. How do you define</p> <p>23 that?</p> <p>24 A I define weak as something that is above</p> <p>25 one, but lower than two, and that the strength of</p>

<p style="text-align: right;">Page 154</p> <p>1 the association is such that the results of the</p> <p>2 study could still be due to random chance, recall</p> <p>3 bias, or confounds within the study.</p> <p>4 Q If you look at a body of literature and</p> <p>5 it's greater than one, and statistically</p> <p>6 significant, but does not approach a point estimate</p> <p>7 of 2.0, you deem that weak literature?</p> <p>8 MS. CURRY: Objection.</p> <p>9 THE WITNESS: No, I would deem that weak</p> <p>10 statistical association, a weak odds ratio. Not</p> <p>11 weak literature, that's not what I said.</p> <p>12 BY MS. GARBER:</p> <p>13 Q Okay. You deem that a weak association?</p> <p>14 A Correct.</p> <p>15 Q And what published peer review study,</p> <p>16 article, text, or treatise do you have that supports</p> <p>17 that statement?</p> <p>18 A So off the top of my head, I can't</p> <p>19 necessarily recall one specific. This is something</p> <p>20 that I've just been taught over the years in</p> <p>21 reviewing epidemiologic literature that you don't</p> <p>22 just look at one thing, i.e., the odds ratio, and</p> <p>23 say, whether or not that proves causation.</p> <p>24 There has to be other things that would</p> <p>25 support the contention of the hypothesis that would</p>	<p style="text-align: right;">Page 156</p> <p>1 epidemiologic textbook in my recollection right now.</p> <p>2 Q I didn't ask you for a textbook. I asked</p> <p>3 you for any source, and you can't name one, can you?</p> <p>4 A As we sit here today, ma'am, I cannot</p> <p>5 recall one for you.</p> <p>6 MS. CURRY: Object to the form.</p> <p>7 BY MS. GARBER:</p> <p>8 Q Do you believe that the plaintiff expert</p> <p>9 reports that you reviewed discussed biologically</p> <p>10 plausible mechanisms of carcinogenicity based on the</p> <p>11 scientific data that they reviewed?</p> <p>12 MS. CURRY: Object to the form.</p> <p>13 BY MS. GARBER:</p> <p>14 Q Whether or not you agree with it, do you</p> <p>15 agree that plaintiff's expert reports discuss</p> <p>16 biologically plausible mechanisms of carcinogenicity</p> <p>17 that were based on scientific data that they</p> <p>18 reviewed?</p> <p>19 MS. CURRY: Object to the form.</p> <p>20 THE WITNESS: Which reports specifically</p> <p>21 are we talking about?</p> <p>22 BY MS. GARBER:</p> <p>23 Q Any of them that you reviewed.</p> <p>24 MS. CURRY: Object to the form.</p> <p>25 THE WITNESS: The various reports had</p>
<p style="text-align: right;">Page 155</p> <p>1 allow you to evaluate whether or not that odds risk</p> <p>2 is impactful, meaningful, but just simply looking at</p> <p>3 the odds ratio is not enough.</p> <p>4 Q Dr. Saenz, point me to one source that</p> <p>5 says that you need a 2.0 point estimate or the study</p> <p>6 data is weak. Just point me to one, just one</p> <p>7 source.</p> <p>8 MS. CURRY: Object to the form.</p> <p>9 MS. GARBER: That says that.</p> <p>10 THE WITNESS: So I actually think that</p> <p>11 within the context of one of the IARC monographs</p> <p>12 they talk about this, the statistical calculations</p> <p>13 for some of the different risk factors, especially</p> <p>14 with talc and the development of ovarian cancer.</p> <p>15 And it's weak, and I believe their term is weak. I</p> <p>16 believe that IARC uses the term weak when we talk</p> <p>17 about statistical associations and odd ratios of 1.2</p> <p>18 and 1.3.</p> <p>19 BY MS. GARBER:</p> <p>20 Q That's not way asked you, did I? What</p> <p>21 did I ask you?</p> <p>22 A I believe that's what you asked you.</p> <p>23 Q Didn't I ask you for a source that says</p> <p>24 that anything below a 2.0 is deemed to be weak?</p> <p>25 A So I don't off the top of my head have an</p>	<p style="text-align: right;">Page 157</p> <p>1 different discussion of different things. So</p> <p>2 without seeing a specific report in front of me, I</p> <p>3 can't assign a name to that topic matter.</p> <p>4 BY MS. GARBER:</p> <p>5 Q How about the gynecologic oncologist</p> <p>6 experts of plaintiffs that you reviewed, did each of</p> <p>7 them discuss biologically plausible mechanisms of</p> <p>8 carcinogenicity based on scientific data that they</p> <p>9 reviewed?</p> <p>10 MS. CURRY: Object to the form.</p> <p>11 THE WITNESS: I do know that one or two</p> <p>12 or perhaps all three of them did. I just don't know</p> <p>13 specifically which ones did. I do believe that they</p> <p>14 had a discussion of biologic plausibility, which I</p> <p>15 disagreed with.</p> <p>16 BY MS. GARBER:</p> <p>17 Q While I know that you disagree with</p> <p>18 plaintiff's experts' causation opinions, do you</p> <p>19 acknowledge that their opinions were based on</p> <p>20 informed scientific medical judgment?</p> <p>21 MS. CURRY: Object to the form.</p> <p>22 THE WITNESS: No.</p> <p>23 MS. GARBER: Are you laughing,</p> <p>24 Ms. Sharko? That seems very unprofessional to me.</p> <p>25 MS. SHARKO: Well, I think your question</p>

<p>Page 158</p> <p>1 is totally misleading and very unprofessional, and 2 I'm trying to honor your request that only one 3 lawyer object. But it's really unclear to me 4 whether you're asking her about the content or 5 whether she agrees with them. 6 MS. GARBER: Well -- 7 MS. SHARKO: I think -- 8 MS. GARBER: -- all I heard was a laugh 9 of my question and I don't think in all my years of 10 taking depositions I've ever had defense counsel 11 laugh out loud at one of my questions. So that's a 12 first for me, so I appreciate that. 13 MS. SHARKO: Well, I think -- 14 MS. GARBER: Go ahead, Dr. Saenz -- 15 MS. SHARKO: -- the record will reflect 16 that you are totally exaggerating what I did. But, 17 go ahead with what you're doing, if that's what you 18 want to do. 19 BY MS. GARBER: 20 Q Dr. Saenz, while you do not agree with 21 plaintiff's experts' causation opinions, do you 22 acknowledge that their opinions were based on 23 informed scientific medical judgment? 24 MS. CURRY: Object to the form. 25 THE WITNESS: So, no, actually. I think</p>	<p>Page 160</p> <p>1 MS. CURRY: Object to the form. 2 THE WITNESS: I believe all three of them 3 are uninformed. 4 BY MS. GARBER: 5 Q All three who? 6 A Drs. Wolf, Blair Smith, and 7 Clarke-Pearson. 8 Q Why were all three of those plaintiff's 9 experts' opinions uninformed? 10 A Because they all concluded that perineal 11 application of talc causes ovarian cancer. 12 Q Did they base their opinions on a review 13 of published literature which included 14 epidemiological and mechanistic data? 15 MS. CURRY: Object to the form. 16 THE WITNESS: Not always. 17 BY MS. GARBER: 18 Q Did Dr. Wolf, Blair Smith, and can I call 19 Dr. CP -- Dr. Clarke-Pearson, CP, Dr. CP for short? 20 A No, you have to call him DCP. That's 21 what we call him. 22 Q So DCP. Did they base their opinions on 23 medical judgment? 24 MS. CURRY: Object to the form. 25 THE WITNESS: Not always.</p>
<p>Page 159</p> <p>1 there's very little evidence for what they put forth 2 as biologic plausibility. I think a lot of your 3 experts' reports were conjecture, hypothesis without 4 any scientific basis. 5 BY MS. GARBER: 6 Q Do you think their opinions were 7 uninformed? 8 MS. CURRY: Object to the form. 9 THE WITNESS: I think their opinions were 10 wrong. 11 BY MS. GARBER: 12 Q That's very different question. You 13 disagree. They're wrong. But were they uninformed? 14 MS. CURRY: Object to the form. 15 THE WITNESS: I think that their opinions 16 were uninformed. I don't think that they based on 17 their opinions on the literature as published, 18 because I think that had they actually read the 19 literature and analyzed it in the manner that I 20 have, they would come to the same conclusion that I 21 have. 22 BY MS. GARBER: 23 Q Tell me which experts' you believe 24 opinions were uninformed and the reason they were 25 uninformed.</p>	<p>Page 161</p> <p>1 BY MS. GARBER: 2 Q What basis do you have to say they didn't 3 base their opinions on medical judgment? 4 A I read their reports and I read their 5 depositions and there were times that what they 6 stated in their reports and their depositions was 7 unsupported by medical judgment. 8 Q Which specifically are you thinking of 9 when you say that? 10 A I would need to see the reports or 11 actually look at my reports and I could tell you 12 where I reference and critique what they said in 13 their reports. 14 Q And so that's what I want to get to. 15 Your critique of those three plaintiff experts are 16 limited to what is referenced in your expert report; 17 is that fair? 18 A No. Also in their depositions as well. 19 Q We'll get to that, but as you sit here, 20 what criticisms do you have of Dr. Wolf aside from 21 what you have referenced in your expert report? 22 MS. CURRY: Object to the form. Do you 23 have a copy of her deposition transcript and her 24 report? 25 ///</p>

Page 162

1 BY MS. GARBER:
2 Q Go ahead, Doctor, do you understand my
3 question?
4 A I can't just give you something broadly.
5 I've done a lot of reading for my preparation to be
6 here and I don't want to misquote her. So I would
7 need to look at the actual report or deposition in
8 order to make sure that I'm giving you a complete
9 reference of -- just basically comprehensive review
10 of what my critiques are.
11 Q And, Doctor, does anything come to mind?
12 A Other than what I've already referenced
13 in my report, additional findings, not off the top
14 of my head, ma'am. I would need to see the
15 documents.
16 Q What about Dr. Smith?
17 A Same thing.
18 Q What about doctor -- DCP?
19 A Same thing.
20 Q And you understand that this is my
21 opportunity to get all of your opinions and
22 criticisms and bases for those opinions; correct?
23 A I understand that.
24 Q And you know I have seven hours. So for
25 me to sit and watch you read a deposition would be

Page 163

1 wholly unfair of each of those witnesses; right?
2 MS. CURRY: Object to the form.
3 THE WITNESS: So my position, ma'am, is
4 that you want me to give you a comprehensive honest
5 answer and in order to do that, I would need the
6 document in front of me.
7 BY MS. GARBER:
8 Q But you can't think of any other
9 criticisms as you sit here today?
10 MS. CURRY: Object to the form.
11 MS. GARBER: Correct?
12 THE WITNESS: Off the top of my head,
13 ma'am, no.
14 BY MS. GARBER:
15 Q So before you read Dr. Wolf's expert
16 report and deposition, did you know her
17 professionally?
18 A No.
19 Q Had you ever heard of her?
20 A No.
21 Q And what about Dr. Smith?
22 A No.
23 Q And obviously you knew DCP?
24 A Correct.
25 Q And you know him professionally?

Page 164

1 A Yes.
2 Q What are the circumstances?
3 A What are the circumstances?
4 Q Uh-huh. How do you know him personally?
5 A We're both gynecologic oncologists. I
6 believe that I have served -- I don't know exactly
7 when. I think I actually might have been on the
8 program committee when he was president of SGO. I
9 think that he and I have done some work together for
10 the Foundation for Women's Cancer as well. I think
11 we might have served on the board at the same time.
12 I don't have an exact recollection, but I think
13 that's quite possible.
14 Q Does he enjoy an excellent professional
15 reputation?
16 MS. CURRY: Object to the form.
17 THE WITNESS: I believe so.
18 BY MS. GARBER:
19 Q Do you respect him?
20 MS. CURRY: Object to the form.
21 THE WITNESS: Not with respect to this
22 matter, ma'am.
23 BY MS. GARBER:
24 Q You respected him before you got involved
25 in this talc case?

Page 165

1 A I still respect him as an individual. I
2 don't respect his opinion with respect to talc in
3 the development of ovarian cancer.
4 Q Doctors can look at the same evidence and
5 come to different medical judgments, can't they?
6 MS. CURRY: Object to the form.
7 THE WITNESS: I don't believe that's
8 true, ma'am. I believe that anybody that has gone
9 as thorough analysis of this literature and looked
10 at all of the considerations would not draw any
11 conclusion other than the conclusion that I have
12 drawn.
13 BY MS. GARBER:
14 Q What is the purpose of a second medical
15 opinion then?
16 A What is the purpose of a second medical
17 opinion?
18 MS. CURRY: Object to the form.
19 THE WITNESS: It varies. Sometimes
20 patients want to know that what their doctor is
21 saying is accurate and true. Other times, patients
22 maybe don't hit it off personality-wise with a
23 certain practitioner and so they want to establish
24 care with someone else.
25 ///

<p style="text-align: right;">Page 166</p> <p>1 BY MS. GARBER:</p> <p>2 Q And sometimes they seek a second medical</p> <p>3 opinion because two doctors can look at the same set</p> <p>4 of evidence and come to different conclusions;</p> <p>5 correct?</p> <p>6 MS. CURRY: Object to the form.</p> <p>7 THE WITNESS: I don't actually think</p> <p>8 that's why you see a second opinion. I think you</p> <p>9 see a second opinion to make sure that you're</p> <p>10 exploring all possible alternatives.</p> <p>11 BY MS. GARBER:</p> <p>12 Q Do you think expert witnesses can weigh</p> <p>13 evidence differently?</p> <p>14 MS. CURRY: Object to the form.</p> <p>15 THE WITNESS: Can you define for me what</p> <p>16 you mean by "weigh"?</p> <p>17 BY MS. GARBER:</p> <p>18 Q Sure. Did you weigh the evidence in your</p> <p>19 expert report? I didn't see where you had done</p> <p>20 that.</p> <p>21 MS. CURRY: Object to the form.</p> <p>22 THE WITNESS: Again, can you --</p> <p>23 BY MS. GARBER:</p> <p>24 Q Did you weigh it in your mind?</p> <p>25 MS. CURRY: Object to the form.</p>	<p style="text-align: right;">Page 168</p> <p>1 from a mechanistic standpoint, and not hypothesized</p> <p>2 about things that don't actually exist, there is</p> <p>3 only one conclusion that can be drawn.</p> <p>4 BY MS. GARBER:</p> <p>5 Q There are scientific bodies that have</p> <p>6 concluded that talc can cause ovarian cancer; true?</p> <p>7 MS. CURRY: Object to the form.</p> <p>8 THE WITNESS: I don't believe that that's</p> <p>9 true.</p> <p>10 BY MS. GARBER:</p> <p>11 Q You don't?</p> <p>12 A No, I don't.</p> <p>13 Q You don't think Health Canada has come to</p> <p>14 that conclusion?</p> <p>15 A No, I absolutely don't. That's a draft</p> <p>16 screening and I don't believe that they have come to</p> <p>17 the conclusion that talc applied in the perineum can</p> <p>18 cause ovarian cancer.</p> <p>19 Q Do you believe that IARC has concluded</p> <p>20 that talc is a possible carcinogen?</p> <p>21 A IARC has classified talc in the perineal</p> <p>22 application as Group 2B, which is possibly</p> <p>23 carcinogenic. That's not saying that talc causes</p> <p>24 ovarian cancer.</p> <p>25 Q You disagree with that assessment?</p>
<p style="text-align: right;">Page 167</p> <p>1 THE WITNESS: What do you mean by</p> <p>2 "weigh"?</p> <p>3 BY MS. GARBER:</p> <p>4 Q So if you looked at say the cohort</p> <p>5 studies versus the case control studies, did you</p> <p>6 weigh the case control less heavily than you weighed</p> <p>7 the cohort studies?</p> <p>8 Did you put any more emphasis on one type</p> <p>9 of evidence as opposed to another?</p> <p>10 A So I wouldn't use the word weigh. I do</p> <p>11 believe that the cohort studies have more scientific</p> <p>12 credibility than the case control studies because</p> <p>13 the case control studies are subject to more biases</p> <p>14 and potential confounds than the cohort studies.</p> <p>15 Q You didn't perform a weight of the</p> <p>16 evidence analysis in your expert report, did you?</p> <p>17 A No, I did not.</p> <p>18 Q Coming to a different conclusion doesn't</p> <p>19 mean the methodology is flawed or improper, does it?</p> <p>20 MS. CURRY: Object to the form.</p> <p>21 THE WITNESS: So in this particular</p> <p>22 matter I believe that it is. I believe that in this</p> <p>23 particular matter, if you've reviewed all of the</p> <p>24 literature, looked at the data that is actually</p> <p>25 available from a biologic plausibility standpoint,</p>	<p style="text-align: right;">Page 169</p> <p>1 A No, I disagree with your statement that</p> <p>2 that says that talc is causing ovarian cancer.</p> <p>3 Q Well, you disagree with IARC's 2012</p> <p>4 assessment of asbestos in fibrous talc. Do you</p> <p>5 disagree with IARC's 2010 and 2006 assessment of</p> <p>6 non-asbestiform talc?</p> <p>7 MS. CURRY: Object to the form, misstates</p> <p>8 prior testimony.</p> <p>9 THE WITNESS: I don't agree that talc</p> <p>10 causes ovarian cancer. So -- and I do believe that</p> <p>11 there's more literature that has become available</p> <p>12 since IARC did its analysis. So yeah, I don't think</p> <p>13 that ovarian cancer even is possibly caused by</p> <p>14 perineal application of talc.</p> <p>15 BY MS. GARBER:</p> <p>16 Q So you think IARC is wrong with regard to</p> <p>17 non-asbestiform talc?</p> <p>18 A I think IARC is wrong. Talc does not</p> <p>19 possibly lead to ovarian cancer. I think IARC is</p> <p>20 wrong.</p> <p>21 Q Has talc been shown to be safe?</p> <p>22 MS. CURRY: Object to the form.</p> <p>23 THE WITNESS: Has talc been shown to be</p> <p>24 safe in what context?</p> <p>25 ///</p>

<p style="text-align: right;">Page 170</p> <p>1 BY MS. GARBER:</p> <p>2 Q In not causing ovarian cancer.</p> <p>3 A I don't know how you would prove a</p> <p>4 negative hypothesis, ma'am.</p> <p>5 Q Can you think of any data that has shown</p> <p>6 that talc is safe?</p> <p>7 MS. CURRY: Object to the form.</p> <p>8 THE WITNESS: In terms of causing ovarian</p> <p>9 cancer?</p> <p>10 MS. GARBER: We'll start there.</p> <p>11 THE WITNESS: I don't believe that any</p> <p>12 such literature exists.</p> <p>13 BY MS. GARBER:</p> <p>14 Q On page eight of your expert report --</p> <p>15 A I'm sorry, what page?</p> <p>16 Q Page eight.</p> <p>17 A Okay.</p> <p>18 Q Which is Exhibit 5. It seems to indicate</p> <p>19 that your opinion is the scientific evidence does</p> <p>20 not support a causal role in the development of</p> <p>21 ovarian cancer with the application of talcum powder</p> <p>22 products applied to the genital region.</p> <p>23 Is that a fair assessment of your report</p> <p>24 on that page?</p> <p>25 MS. CURRY: You're reading -- I'm just</p>	<p style="text-align: right;">Page 172</p> <p>1 Q Is that still your opinion?</p> <p>2 A That is still my opinion.</p> <p>3 Q And in coming to that opinion as stated</p> <p>4 in your report, you did not review the totality of</p> <p>5 relevant literature, did you?</p> <p>6 MS. CURRY: Object to the form.</p> <p>7 THE WITNESS: I don't believe that's</p> <p>8 correct.</p> <p>9 BY MS. GARBER:</p> <p>10 Q Are the articles cited in the four</p> <p>11 corners of your report given any more weight than</p> <p>12 the articles that are not cited there?</p> <p>13 MS. CURRY: Object to the form.</p> <p>14 THE WITNESS: So everything that I've</p> <p>15 read, everything that I've evaluated is in my</p> <p>16 report. If there's a particular article that you're</p> <p>17 referencing to that you think I've left out, I'd be</p> <p>18 happy to look at it right now.</p> <p>19 BY MS. GARBER:</p> <p>20 Q Do you think in coming to a causation</p> <p>21 opinion, it's important to review the totality of</p> <p>22 the relevant evidence as to the topic?</p> <p>23 MS. CURRY: Object to the form.</p> <p>24 THE WITNESS: I believe that I have</p> <p>25 reviewed a very comprehensive breadth and depth of</p>
<p style="text-align: right;">Page 171</p> <p>1 trying to follow along with you.</p> <p>2 MS. GARBER: Under the genital</p> <p>3 application of talc and risk factor of ovarian</p> <p>4 cancer overview.</p> <p>5 BY MS. GARBER:</p> <p>6 Q Is it your opinion that the scientific</p> <p>7 evidence does not support a causal role in the</p> <p>8 development of ovarian cancer with the application</p> <p>9 of talc to the perineal region?</p> <p>10 Does your report say that?</p> <p>11 A Are we referring something specific --</p> <p>12 Q Yeah, your report, your report, Doctor.</p> <p>13 A Can you refer me, ma'am, to exactly where</p> <p>14 you're reading or are we doing a general statement?</p> <p>15 Q In the first paragraph under the heading</p> <p>16 I just read.</p> <p>17 A Okay.</p> <p>18 Q Is that your opinion?</p> <p>19 A Which sentence are we starting with?</p> <p>20 Q The second sentence.</p> <p>21 A Okay. So I write, "despite many years of</p> <p>22 research on this topic, the scientific evidence does</p> <p>23 not support a causal role in the development of</p> <p>24 ovarian cancer, with application of talc to the</p> <p>25 perineal region." Right.</p>	<p style="text-align: right;">Page 173</p> <p>1 the literature that is available on this topic.</p> <p>2 BY MS. GARBER:</p> <p>3 Q And in looking at the topic of whether or</p> <p>4 not an exposure can cause cancer, I like to call</p> <p>5 them little -- different buckets of evidence.</p> <p>6 So would you agree that in looking at</p> <p>7 that assessment, it would be important to look at</p> <p>8 the human epidemiological literature?</p> <p>9 A Yes, and I have.</p> <p>10 Q And the totality of that literature;</p> <p>11 correct?</p> <p>12 A Yes, and I have.</p> <p>13 Q And it would be important to look at the</p> <p>14 mechanistic data or the biologically plausible</p> <p>15 mechanisms by which that agent or exposure could</p> <p>16 cause cancer; correct?</p> <p>17 A Yes, and I have. And the hypothesis here</p> <p>18 is that chronic inflammation from the talc is</p> <p>19 leading to the development of ovarian cancer, and</p> <p>20 I've looked at that literature and I don't believe</p> <p>21 that that is supported.</p> <p>22 Q You believe that you've looked at the</p> <p>23 full body of the literature that speaks to the issue</p> <p>24 of talc and inflammation in its role in causing</p> <p>25 cancer, you believe you've looked at that full body</p>

<p style="text-align: right;">Page 174</p> <p>1 of the literature?</p> <p>2 MS. CURRY: Object to the form.</p> <p>3 THE WITNESS: In its role in causing</p> <p>4 ovarian cancer; yes.</p> <p>5 BY MS. GARBER:</p> <p>6 Q And do you believe that you've looked at</p> <p>7 the full body of the literature that shows the</p> <p>8 mechanistic ways in which inflammation can cause</p> <p>9 ovarian cancer?</p> <p>10 MS. CURRY: Object to the form.</p> <p>11 BY MS. GARBER:</p> <p>12 Q In other words, the pathways in which</p> <p>13 inflammation can cause ovarian cancer?</p> <p>14 MS. CURRY: Object to the form.</p> <p>15 THE WITNESS: I believe that I've</p> <p>16 thoroughly reviewed the hypothesis that chronic</p> <p>17 inflammation can cause ovarian cancer or lead to the</p> <p>18 development of ovarian cancer and I don't believe</p> <p>19 that it is substantiated by the published</p> <p>20 literature.</p> <p>21 BY MS. GARBER:</p> <p>22 Q Let's talk about oxidative stress.</p> <p>23 A Okay.</p> <p>24 Q Is oxidative stress thought to be a</p> <p>25 mechanism by which an agent or in general can result</p>	<p style="text-align: right;">Page 176</p> <p>1 A Dr. Saed's 2019 paper is in his report</p> <p>2 and I have reviewed his report. Dr. Saed does not</p> <p>3 ever demonstrate that generation of oxidative</p> <p>4 species leads to malignant transformation.</p> <p>5 Q That's based on not reviewing his actual</p> <p>6 published paper, but rather his expert report in</p> <p>7 this case?</p> <p>8 MS. CURRY: Object to the form.</p> <p>9 MS. GARBER: Correct?</p> <p>10 THE WITNESS: Ma'am, his expert report is</p> <p>11 what he's putting forth for his opinion to say that</p> <p>12 this exists. I've read his expert report. There is</p> <p>13 generation of oxidative stress responses. There is</p> <p>14 no data that that leads to malignant transformation.</p> <p>15 BY MS. GARBER:</p> <p>16 Q Have you read the Shukla 2009 paper?</p> <p>17 A No, I have not.</p> <p>18 Q So you would have no basis to know</p> <p>19 whether or not those papers provided mechanistic</p> <p>20 data as to the connection between talc and ovarian</p> <p>21 cancer or other forms of paper, because you've never</p> <p>22 read them, right?</p> <p>23 MS. CURRY: Object to the form.</p> <p>24 THE WITNESS: There's no data, ma'am, in</p> <p>25 the published literature that demonstrates that the</p>
<p style="text-align: right;">Page 175</p> <p>1 in cancer, just speaking broad picture?</p> <p>2 A Speaking --</p> <p>3 MS. CURRY: Object to the form.</p> <p>4 THE WITNESS: Speaking broad picture,</p> <p>5 oxidative stress can be a response to any particular</p> <p>6 stressful situation. Inflammation is a generalized</p> <p>7 process that's not necessarily carcinogenic.</p> <p>8 BY MS. GARBER:</p> <p>9 Q But oxidative stress is a mechanism</p> <p>10 that's understood in the medical community; correct?</p> <p>11 A Yes.</p> <p>12 MS. CURRY: Object to the form.</p> <p>13 THE WITNESS: But not in the sense of</p> <p>14 oxidative stress leading to malignant transformation</p> <p>15 in ovarian cancer. There is no literature that</p> <p>16 supports that.</p> <p>17 BY MS. GARBER:</p> <p>18 Q There's no literature at all?</p> <p>19 A There's no literature that supports</p> <p>20 mutagenicity as a result of the generation of</p> <p>21 oxidative species in ovarian cancer.</p> <p>22 Q Have you reviewed the Buz'Zard paper?</p> <p>23 A No, I've not reviewed that paper.</p> <p>24 Q Have you -- and you haven't reviewed</p> <p>25 Dr. Saed's 2019 paper, have you?</p>	<p style="text-align: right;">Page 177</p> <p>1 generation of oxidative stress, reactive oxygen</p> <p>2 species or nitrogen species leads to malignant</p> <p>3 transformation.</p> <p>4 BY MS. GARBER:</p> <p>5 Q That's not my question. Have you read</p> <p>6 the -- no, strike that.</p> <p>7 You have not read the Shukla 2009 paper;</p> <p>8 correct?</p> <p>9 A Correct.</p> <p>10 Q You have not read the Buz'Zard 2007</p> <p>11 paper; correct?</p> <p>12 A Correct.</p> <p>13 Q And you have not read the Saed 2019</p> <p>14 published paper; correct?</p> <p>15 A Ma'am, this Saed 2019 paper is in his</p> <p>16 report. So the content of that paper I have read.</p> <p>17 There is no generation of malignant cells in that</p> <p>18 report.</p> <p>19 MS. GARBER: Motion to strike as</p> <p>20 nonresponsive.</p> <p>21 BY MS. GARBER:</p> <p>22 Q I just need a yes-or-no question [sic.].</p> <p>23 A It's not a yes-or-no answer.</p> <p>24 Q Have you read the paper or not?</p> <p>25 MS. CURRY: Object to the form.</p>

<p style="text-align: right;">Page 178</p> <p>1 THE WITNESS: I've read his report. His 2 report details his paper. 3 MS. GARBER: We'll get to his paper. 4 BY MS. GARBER: 5 Q Doctor, you have not considered the 6 Shukla, Saed 2019 paper, or the Buz'Zard 2007 paper 7 in connection with your opinions; is that a true 8 statement? 9 MS. CURRY: Object to the form. 10 THE WITNESS: No, that's incorrect. 11 BY MS. GARBER: 12 Q Because the Saed paper was contained 13 within his expert report, that's your testimony? 14 A That is my testimony. 15 Q Do you know what the findings were of the 16 Buz'Zard paper? 17 A No, ma'am. 18 Q Do you know what the findings were of the 19 Shukla paper? 20 A I have a vague sense, just based on 21 reading other expert reports, that both of those 22 papers involved inflammation, but I also have a 23 vague sense that neither of those papers involved 24 malignant transformation. But I've not read either 25 of those reports.</p>	<p style="text-align: right;">Page 180</p> <p>1 Q Did you ask for that testing from defense 2 counsel? 3 A I did not. 4 Q Why not? 5 A Because I don't believe that it is 6 germane to my opinion, which based on what we've 7 already talked about before. 8 Q You don't need to know whether or not 9 asbestos is contained in Johnson & Johnson's baby 10 powder products? 11 A I don't, because if baby powder contained 12 asbestos or not is irrelevant to the fact that the 13 literature does not support that perineal 14 application of talc leads to an increased risk of 15 developing ovarian cancer. 16 Q Why do you think the United States 17 government is so interested to know if Johnson & 18 Johnson's baby powder products contain asbestos? Do 19 you think they want to know that because it doesn't 20 matter? 21 MS. CURRY: Object to the form. 22 THE WITNESS: I don't think that has 23 anything to do with the scientific medical question 24 that we're dealing with right here right now, ma'am. 25 ///</p>
<p style="text-align: right;">Page 179</p> <p>1 Q What was your basis for your vague 2 recollection of those papers? 3 A Reading other expert reports, including 4 Dr. Saed's report, including some of the other 5 expert reports for plaintiff's side that reference 6 those papers. 7 Q So we're here in a case wherein experts 8 have said that talcum powder products can cause 9 ovarian cancer, a very lethal cancer, and you are 10 aware of literature, and you're telling me you did 11 not review that literature. 12 MS. CURRY: Object to the form. 13 THE WITNESS: What I'm telling you, 14 ma'am, is that there is no literature that 15 demonstrates malignant transformation. So have I 16 read every single paper ever published on anything? 17 No. But I do know that there is no published 18 literature that demonstrates that talc leads to 19 malignant transformation in ovarian cells. 20 BY MS. GARBER: 21 Q In reading the other expert reports, did 22 you review or read about Dr. Longo's testing for 23 talcum powder products and asbestos content? 24 A I did see other experts make mention of 25 that report.</p>	<p style="text-align: right;">Page 181</p> <p>1 BY MS. GARBER: 2 Q Doctor, in your report, you fail to 3 address or discuss the poor study designs and 4 limitations of the cohort studies, don't you? 5 MS. CURRY: Object to the form. 6 THE WITNESS: I don't think I failed to 7 evaluate any of the studies that are in my report. 8 BY MS. GARBER: 9 Q Do you discuss the study of limitations 10 in the cohort studies? 11 A I don't discuss the limitations that are 12 in the cohort studies because the authors do that 13 themselves in their discussion sections. 14 Q Don't you think it's important to 15 consider what the author says is the limitations of 16 those data in formulating your opinion? 17 MS. CURRY: Object to the form. 18 THE WITNESS: I did consider it. I 19 considered it when I read the paper and that's what 20 allowed me to formulate my opinions. 21 BY MS. GARBER: 22 Q In formulating your opinions, are they 23 based on fact that you believe the cohort studies do 24 not show an association between genital talcum 25 powder use and epithelial ovarian cancer?</p>

<p style="text-align: right;">Page 182</p> <p>1 MS. CURRY: Object to the form.</p> <p>2 THE WITNESS: That's part of the data</p> <p>3 that I used to formulate my opinions.</p> <p>4 BY MS. GARBER:</p> <p>5 Q In formulating your opinions, I didn't</p> <p>6 see any analysis in your report addressing the</p> <p>7 opinions of the Health Canada assessment; is that</p> <p>8 true?</p> <p>9 A So I believe that the Health Canada</p> <p>10 assessment is primarily based off of the Taher</p> <p>11 publishing -- actually, I take that back. The Taher</p> <p>12 manuscript, because Taher has not been published.</p> <p>13 And so I don't know whether or not that actually</p> <p>14 will be published; it's not something that's peer</p> <p>15 reviewed.</p> <p>16 And the Health Canada assessment as I</p> <p>17 understand it is a draft. That's not necessarily</p> <p>18 published peer-reviewed literature either. So</p> <p>19 although I read it and I read Taher, I did not put</p> <p>20 it into my analysis, because I don't think it adds</p> <p>21 anything to the discussion that is already</p> <p>22 incorporated in my report.</p> <p>23 Q If both of those papers were peer</p> <p>24 reviewed and published -- I know that the Health</p> <p>25 Canada wouldn't be peer reviewed and published, but</p>	<p style="text-align: right;">Page 184</p> <p>1 you?</p> <p>2 A As a separate paragraph? No, I don't</p> <p>3 have a methodology section as a separate paragraph,</p> <p>4 but the details of the analysis that I did are</p> <p>5 certainly in the four corners of the report.</p> <p>6 Q Doctor, nowhere in your expert report do</p> <p>7 you even utilize the word "methodology," do you?</p> <p>8 A I don't know that's necessarily true.</p> <p>9 Q Doctor, isn't the point of stating what</p> <p>10 your causation methodology is, so that your opinions</p> <p>11 can be reproduced?</p> <p>12 MS. CURRY: Object to the form.</p> <p>13 THE WITNESS: So every single paper that</p> <p>14 I read, every single opinion that I had, why I came</p> <p>15 to the conclusions that I came to, is all in the</p> <p>16 body of the report.</p> <p>17 BY MS. GARBER:</p> <p>18 Q It is?</p> <p>19 A Yes, it is.</p> <p>20 Q Okay. Can you point to me with regard to</p> <p>21 the literature about how particulates have been</p> <p>22 shown to translocate to reach the ovary?</p> <p>23 Can you show me where you are discussing</p> <p>24 every one of those literature, your conclusions</p> <p>25 about those literature, and why you concluded the</p>
<p style="text-align: right;">Page 183</p> <p>1 if it was a final draft and it made the exact same</p> <p>2 conclusions and the Taher paper made the exact same</p> <p>3 conclusions, would that change your expert opinion</p> <p>4 in this case?</p> <p>5 MS. CURRY: Object to the form.</p> <p>6 THE WITNESS: No, because I actually</p> <p>7 don't think Taher adds anything to the analysis.</p> <p>8 It's much the same data that was in Berge and in</p> <p>9 Penninkilampi.</p> <p>10 BY MS. GARBER:</p> <p>11 Q In your critique of -- is it true,</p> <p>12 Doctor, that in the four corners of your expert</p> <p>13 report you do not state anywhere the methodology</p> <p>14 that you employed in coming to your causation</p> <p>15 opinion?</p> <p>16 MS. CURRY: Object to the form.</p> <p>17 THE WITNESS: So I don't think I</p> <p>18 necessarily had a paragraph that says exactly what I</p> <p>19 did, but I certainly think the breadth and depth of</p> <p>20 the literature I reviewed and the detailed analysis</p> <p>21 of all the literature I reviewed is contained within</p> <p>22 the details of my report.</p> <p>23 BY MS. GARBER:</p> <p>24 Q In the four corners of your expert</p> <p>25 report, you don't have a methodology section, do</p>	<p style="text-align: right;">Page 185</p> <p>1 way you did with regard to those literature?</p> <p>2 MS. CURRY: Object to the form.</p> <p>3 THE WITNESS: Page 28. "The vagina is</p> <p>4 not the perineum, and no studies have ever shown</p> <p>5 that something placed onto the perineum can migrate</p> <p>6 to the ovaries. While plaintiffs' experts discuss</p> <p>7 in their reports that the female reproductive tract</p> <p>8 is open to the external environment, there is not a</p> <p>9 single study that traces something from the vulva to</p> <p>10 the ovaries. Some of plaintiffs' experts rely on</p> <p>11 the study by Drs. Egli and Newton published in 1961</p> <p>12 to support the hypothesis that talc can migrate from</p> <p>13 the perineum to the ovaries."</p> <p>14 I then go on to describe in great detail</p> <p>15 the context of that study and the conditions under</p> <p>16 which it was held. And then I say why I've</p> <p>17 concluded what I concluded.</p> <p>18 BY MS. GARBER:</p> <p>19 Q One study?</p> <p>20 A Ma'am --</p> <p>21 MS. CURRY: Object to the form.</p> <p>22 THE WITNESS: -- you asked me to point</p> <p>23 out one place, so I did it.</p> <p>24 BY MS. GARBER:</p> <p>25 Q Okay. But I think what you told me,</p>

<p style="text-align: right;">Page 186</p> <p>1 Doctor, is that you reviewed the full body of the</p> <p>2 literature and then you analyzed it in your report.</p> <p>3 And I don't see that being done. I see you maybe</p> <p>4 talking about one study or another. I don't see you</p> <p>5 analyzing the data in your report --</p> <p>6 A Okay. So --</p> <p>7 Q -- or providing methodology for the way</p> <p>8 you do it.</p> <p>9 MS. CURRY: Object to the form.</p> <p>10 THE WITNESS: Then I think you're missing</p> <p>11 the context of the report because my report is quite</p> <p>12 extensive. I also reference in my reference list</p> <p>13 the Vantor article which talks about migration of</p> <p>14 particulate radioactive tracer from the vagina to</p> <p>15 the peritoneal cavity and the ovaries.</p> <p>16 So, ma'am, it's there. It's throughout</p> <p>17 the report.</p> <p>18 BY MS. GARBER:</p> <p>19 Q Doctor, can you turn to me in your report</p> <p>20 and tell me where I can read the methodology that</p> <p>21 you employed in coming to your causation opinions?</p> <p>22 MS. CURRY: Object to the form.</p> <p>23 THE WITNESS: Ma'am, you already asked me</p> <p>24 whether or not I have a section on methodology, and</p> <p>25 I told you that I don't have a specific paragraph</p>	<p style="text-align: right;">Page 188</p> <p>1 BY MS. GARBER:</p> <p>2 Q In your critique of plaintiffs' expert's</p> <p>3 opinions, you don't provide your methodology in</p> <p>4 coming to those opinions, do you?</p> <p>5 MS. CURRY: Object to the form.</p> <p>6 THE WITNESS: Ma'am, I just read you a</p> <p>7 section that was from the critique of one of</p> <p>8 plaintiff expert's opinions where I showed you. I</p> <p>9 read an article where it talks about migration of</p> <p>10 particles. I explained the context of that article,</p> <p>11 the conditions under which that study was held, and</p> <p>12 why I, therefore, dispute and disagree with your</p> <p>13 expert.</p> <p>14 That is a thorough explanation of how I</p> <p>15 came to the conclusion that I came to and why I'm</p> <p>16 critical of your expert.</p> <p>17 BY MS. GARBER:</p> <p>18 Q Is that the extent of your methodology?</p> <p>19 MS. CURRY: Object to the form.</p> <p>20 THE WITNESS: Throughout my report,</p> <p>21 ma'am, I'm very thorough in supporting the</p> <p>22 conclusions that I have come to.</p> <p>23 BY MS. GARBER:</p> <p>24 Q Dr. Saenz, can you -- strike that.</p> <p>25 Can you name any causation methodologies</p>
<p style="text-align: right;">Page 187</p> <p>1 titled that. But I do have a demonstration of the</p> <p>2 extent of research that I went through in terms of</p> <p>3 analyzing studies, comparing the known literature to</p> <p>4 what we know based on medical and scientific fact,</p> <p>5 and explaining how I came to the opinions that I</p> <p>6 came to.</p> <p>7 MS. GARBER: Motion to strike as</p> <p>8 nonresponsive.</p> <p>9 BY MS. GARBER:</p> <p>10 Q Doctor, can you please point me to the</p> <p>11 place in your report where you provide for me the</p> <p>12 methodology that you employed in coming to your</p> <p>13 expert opinions?</p> <p>14 MS. CURRY: Object to the form.</p> <p>15 THE WITNESS: Ma'am, I already answered</p> <p>16 this for you.</p> <p>17 BY MS. GARBER:</p> <p>18 Q That was your answer?</p> <p>19 A Yes, ma'am.</p> <p>20 Q In other words, you can't point me to an</p> <p>21 area in your report where you provide the</p> <p>22 methodology, can you?</p> <p>23 MS. CURRY: Object to the form.</p> <p>24 THE WITNESS: Ma'am, I already told you,</p> <p>25 I don't have a specific section titled methodology.</p>	<p style="text-align: right;">Page 189</p> <p>1 that have been peer reviewed and published as a</p> <p>2 scientifically accepted methodology for rendering a</p> <p>3 causation opinion?</p> <p>4 MS. CURRY: Object to the form.</p> <p>5 THE WITNESS: I don't really understand</p> <p>6 what you mean.</p> <p>7 BY MS. GARBER:</p> <p>8 Q Can you think of any peer-reviewed</p> <p>9 methodology that's used by scientists to render</p> <p>10 causation opinions?</p> <p>11 MS. CURRY: Same objection.</p> <p>12 THE WITNESS: So throughout plaintiffs'</p> <p>13 expert's reports, they talk about the Bradford Hill</p> <p>14 criteria and looking at things such as the</p> <p>15 literature, the epidemiologic literature, whether or</p> <p>16 not it supports that, the mechanistic studies,</p> <p>17 biologic plausibility, strength of association,</p> <p>18 consistency in the literature.</p> <p>19 So I do believe that that as a system, if</p> <p>20 you will, is a methodology for trying to define</p> <p>21 causation.</p> <p>22 BY MS. GARBER:</p> <p>23 Q And your understanding is that's peer</p> <p>24 reviewed; correct?</p> <p>25 A I don't necessarily know that Bradford</p>

<p style="text-align: right;">Page 190</p> <p>1 Hill criteria per se was peer reviewed because I've 2 not actually seen the publication. But I do think 3 that is well accepted in the medical and scientific 4 community as criteria by which causation can be 5 evaluated. 6 Q You didn't apply the Bradford Hill in 7 your analysis in coming to your causation opinions 8 in this case, did you? 9 MS. CURRY: Object to the form. 10 THE WITNESS: Oh, I disagree with that 11 completely. I didn't sit there and outline the 12 Bradford Hill criteria by the nine criteria that are 13 listed in the original proposition. However, my 14 analysis itself is the way that I've always analyzed 15 certain questions in looking at it. So the actual 16 concepts of strength of association, consistency in 17 the data, biologic plausibility, that's all there. 18 That's all in my report. 19 So I didn't title it perhaps the way that 20 you wanted me to title it, but the crux of it is all 21 there in my report. 22 BY MS. GARBER: 23 Q Did you think I wanted you to do it in a 24 certain way? 25 A Well, I think --</p>	<p style="text-align: right;">Page 192</p> <p>1 somewhere in your expert report? 2 MS. CURRY: Object to the form. 3 THE WITNESS: So my report is a total 4 report. There are places in there that I absolutely 5 talk about the strength of the association. I 6 absolutely talk about consistency. I absolutely 7 talk about biologic plausibility. I absolutely talk 8 about the mechanisms. 9 So the report is something that's to be 10 accepted in total. It's not like there's one page 11 to pull out and say, oh, this is that. 12 BY MS. GARBER: 13 Q You had me reference or you turned -- 14 strike that. 15 With regard to migration of talc, you had 16 me turn to page 17. Do you remember that? 17 MS. CURRY: Object to the form. 18 THE WITNESS: I don't actually think 19 that's the page I had you turn to. 20 BY MS. GARBER: 21 Q Strike that. Doctor, in your expert 22 report, you discuss migration of talc from the 23 perineum to the ovaries at pages 17 and 18; is that 24 correct? 25 MS. CURRY: Object to the form.</p>
<p style="text-align: right;">Page 191</p> <p>1 MS. CURRY: Object to the form. 2 THE WITNESS: -- there's certain things 3 that you clearly have wanted me to do in a certain 4 way that has come up a couple times now when we've 5 talked about the methodology. So in terms of how 6 I've gone about analyzing this problem, I've 7 analyzed it the same way people go about a Bradford 8 Hill analysis. I just haven't titled it that way. 9 BY MS. GARBER: 10 Q You think that you have shown the reader 11 in the four corners of your expert report a Bradford 12 Hill analysis of the data in coming to your 13 causation opinions? 14 A Absolutely. 15 Q And how am I to find that within the four 16 corners of your report? Where can I find that 17 Bradford Hill analysis? 18 MS. CURRY: Object to the form. 19 THE WITNESS: Read the report. It's 20 throughout the report. 21 BY MS. GARBER: 22 Q So I just have to read the report and 23 figure out where you're talking about the 24 association and whether or not you think it's weak 25 or strong or adequate? I just have to find that</p>	<p style="text-align: right;">Page 193</p> <p>1 THE WITNESS: The topic of this section 2 is titled "Migration of Talc from the Perineum to 3 the Ovaries"; correct. 4 BY MS. GARBER: 5 Q That appears at page -- at half of the 6 page on 17 and a full page at 18; correct? 7 A Yes. 8 Q And, Doctor, in that part of your report, 9 you fail to acknowledge the data in the 10 peer-reviewed and published author statements 11 regarding biologically plausible mechanisms for 12 talcum powder products' migration and its 13 carcinogenicity, don't you? 14 MS. CURRY: Object to the form. 15 THE WITNESS: No, there is no data from 16 migration from the perineum to the ovaries. 17 BY MS. GARBER: 18 Q Are you saying, and are you contending 19 that there is no published data in the peer-reviewed 20 literature which indicates that talc can migrate? 21 A I'm saying there's no data in the 22 peer-reviewed literature that can show that talc can 23 migrate from the perineum to the ovaries. 24 Q Doctor, you're aware that there are many 25 epidemiological studies that have indicated that</p>

<p style="text-align: right;">Page 194</p> <p>1 talc can migrate from the genitals and reach the</p> <p>2 ovaries, you're aware of those data; right?</p> <p>3 MS. CURRY: Object to the form.</p> <p>4 THE WITNESS: No, there are no data that</p> <p>5 show that.</p> <p>6 MS. GARBER: I'm out of the stickers.</p> <p>7 THE REPORTER: Would you like to go off</p> <p>8 the record while I print them up?</p> <p>9 MS. GARBER: Sure.</p> <p>10 THE VIDEOGRAPHER: The time is now 2:09.</p> <p>11 Going off the record.</p> <p>12 (Break in the deposition taken at 2:11 p.m.)</p> <p>13 0o0</p> <p>14 (The deposition resumed at 2:11 p.m.)</p> <p>15 0o0</p> <p>16 THE VIDEOGRAPHER: The time is now 2:10.</p> <p>17 Back on the record.</p> <p>18 (C. Saenz Exhibit 11 was marked for</p> <p>19 identification.)</p> <p>20 BY MS. GARBER:</p> <p>21 Q Doctor, I'm handing to you what is a</p> <p>22 document that we've marked as Exhibit 11, which is</p> <p>23 titled "Biologic Plausibility Migration</p> <p>24 Translocation."</p> <p>25 Doctor, I will represent to you this is a</p>	<p style="text-align: right;">Page 196</p> <p>1 THE WITNESS: No, because none of these</p> <p>2 quotes is actually scientific proof that talc can</p> <p>3 migrate from the perineum to the ovaries.</p> <p>4 BY MS. GARBER:</p> <p>5 Q Doctor, you understand that the authors</p> <p>6 of these published -- these cited publications in</p> <p>7 Exhibit 11 are statements that were pulled from the</p> <p>8 peer-reviewed, published literature of these study</p> <p>9 authors?</p> <p>10 Do you understand that?</p> <p>11 A I understand --</p> <p>12 MS. CURRY: Object to the form.</p> <p>13 THE WITNESS: I understand that, and not</p> <p>14 a single one of these is actually demonstrating</p> <p>15 proof that talc applied to the perineum can migrate</p> <p>16 to the ovaries. Not a single one.</p> <p>17 In fact, these are described as</p> <p>18 plausibility. These are described as particles up</p> <p>19 here. This is not scientific evidence, ma'am. This</p> <p>20 is your listing pulling one sentences out of</p> <p>21 articles without documented scientific proof of the</p> <p>22 migration path from the perineum to the ovaries.</p> <p>23 BY MS. GARBER:</p> <p>24 Q So, Doctor, do you see the title of the</p> <p>25 this document, as "Biologic Plausibility." Do you</p>
<p style="text-align: right;">Page 195</p> <p>1 document that I created. I will represent to you</p> <p>2 these are quotes from the published literature with</p> <p>3 regard to talc and ovarian cancer.</p> <p>4 Doctor, just -- I don't expect you to</p> <p>5 read every single one of these, but do you have a</p> <p>6 single one of these citations in the four corners of</p> <p>7 your report?</p> <p>8 MS. CURRY: I'm going to object to the</p> <p>9 use of this document as it's literally pulled out</p> <p>10 one sentences, sometimes not even full sentences of</p> <p>11 a variety of different articles without the expert</p> <p>12 witness having the opportunity to actually look at</p> <p>13 the totality of the article, say, that --</p> <p>14 MS. GARBER: I appreciate all that</p> <p>15 testimony, Ms. Curry.</p> <p>16 THE WITNESS: I'm sorry, what's your</p> <p>17 question?</p> <p>18 BY MS. GARBER:</p> <p>19 Q Do you have a single one of these quotes</p> <p>20 from the published literature in your expert report?</p> <p>21 MS. CURRY: And I object to the form of</p> <p>22 the question.</p> <p>23 THE WITNESS: The quotes that you</p> <p>24 yourself pulled and put on this document?</p> <p>25 MS. GARBER: Yes.</p>	<p style="text-align: right;">Page 197</p> <p>1 see that?</p> <p>2 A That's your title.</p> <p>3 Q Yes. Do you know what that means?</p> <p>4 A Yes, I do.</p> <p>5 Q What?</p> <p>6 A That there is the hypothesis of how this</p> <p>7 might actually happen from a biologic standpoint.</p> <p>8 But there isn't a single scientific article that has</p> <p>9 actually ever traced a migratory path of talc from</p> <p>10 the perineum to the ovaries, not a single one, and</p> <p>11 you putting a listing here of these different</p> <p>12 sentences saying, well, this article says it could</p> <p>13 happen doesn't make it so.</p> <p>14 Q Doctor, you've used the word "proof"</p> <p>15 there a couple of times. Is it your understanding</p> <p>16 for biologic plausibility that you need proof?</p> <p>17 MS. CURRY: Object to the form.</p> <p>18 BY MS. GARBER:</p> <p>19 Q Or that it's a plausible mechanism?</p> <p>20 A My understanding --</p> <p>21 MS. CURRY: Object to the form.</p> <p>22 THE WITNESS: My understanding in this</p> <p>23 particular case is that there has to be some proof</p> <p>24 that a particulate matter applied to the perineum</p> <p>25 can actually make it to the ovaries for the</p>

<p style="text-align: right;">Page 198</p> <p>1 hypothesis that talc can cause ovarian cancer to be 2 so. 3 BY MS. GARBER: 4 Q That's your understanding of biologic 5 plausibility? 6 A In this particular circumstance; yes. 7 Q What is your understanding of biologic 8 plausibility in the context of the Bradford Hill 9 guidelines? 10 MS. CURRY: Object to the form. 11 THE WITNESS: My understanding is that 12 there has to be biologic evidence that what you're 13 hypothesizing could actually happen. It doesn't 14 have to be that you have to prove that talc itself 15 could migrate, but there's no studies of any 16 migration whatsoever in the human that any 17 particulate matter applied to the perineum can make 18 it all the way to the ovaries. 19 So it doesn't have to be talc, but it has 20 to show that something can actually make it from the 21 perineum to the ovaries. 22 BY MS. GARBER: 23 Q Let's mark as Exhibit 12 -- Doctor, the 24 point I was trying to make with this Exhibit 11 is 25 this: There are peer-reviewed, published papers</p>	<p style="text-align: right;">Page 200</p> <p>1 THE WITNESS: Some of the case control 2 studies have shown a weak increased odds ratio for 3 the development of ovarian cancer with the perineal 4 application of talc. 5 BY MS. GARBER: 6 Q Some of the meta-analysis, or is it, in 7 fact, all of the meta-analysis, which shows an 8 association between genital talc and the development 9 of epithelial ovarian cancer? 10 A So the meta -- 11 MS. CURRY: Object to the form. 12 THE WITNESS: -- the meta-analyses that 13 have been done only show that when they look at the 14 case control studies. They don't show that when 15 they look at the cohort studies. 16 BY MS. GARBER: 17 Q Okay. Some of the epidemiological data 18 that shows an association between genital 19 application of talc and the development of 20 epithelial ovarian cancer also report that it's 21 biologically plausible that talc can reach the 22 ovaries from the genitals, don't they? 23 A No. 24 MS. CURRY: Object to the form. 25 THE WITNESS: It doesn't. They suppose</p>
<p style="text-align: right;">Page 199</p> <p>1 where the authors concluded that talc can migrate, 2 that it's a biologically plausible mechanism that 3 talc with migrate. 4 Do you disagree with that? 5 MS. CURRY: Object to the form. 6 THE WITNESS: I disagree with the concept 7 that's saying that if it migrates from the vagina to 8 the ovaries, it's the same as migrating from the 9 perineum to the ovaries. 10 BY MS. GARBER: 11 Q That wasn't my question. 12 A But it is, ma'am, because you didn't 13 qualify. You're just saying talc can migrate, 14 period. That's not the same thing. What we're 15 talking about here is whether or not we're including 16 the entire female anatomy, and we have to do that. 17 Having a study show that something can be 18 in the vagina and make it to the ovaries is not the 19 same thing as going from the perineum to the 20 ovaries. 21 Q Let's talk about the epi. The epi 22 studies show that talc applied to the genitals is 23 associated with epithelial ovarian cancer in some of 24 the studies. You'll agree to that; right? 25 MS. CURRY: Object to the form.</p>	<p style="text-align: right;">Page 201</p> <p>1 that. They don't actually show that. 2 BY MS. GARBER: 3 Q But that's the authors' conclusions, that 4 it can get there. They think it's biologically 5 plausible? 6 MS. CURRY: Object to the form. 7 THE WITNESS: But there's no data for 8 that. They can conclude that, but there's no data 9 for that. There has to be data for which to support 10 that hypothesis. And there's not. 11 BY MS. GARBER: 12 Q Doctor, in the peer-review process, a 13 study author who is looking at the data of genital 14 application of talc and development of ovarian 15 cancer is saying it's biologically plausible that 16 talc can go from the genitals to the ovaries, and 17 that's been peer reviewed and published, do you 18 agree with that? 19 MS. CURRY: Object to the form. 20 THE WITNESS: I don't agree with that 21 statement. 22 BY MS GARBER: 23 Q No, I know you don't agree with the -- 24 with the conclusion. But do you agree that a study 25 author who studied the topic has concluded it's</p>

<p style="text-align: right;">Page 202</p> <p>1 biologically plausible.</p> <p>2 A There's always evidence, and in fact --</p> <p>3 Q Doctor, it's a yes-or-no question --</p> <p>4 A No, it's not, ma'am.</p> <p>5 MS. CURRY: Object to the form.</p> <p>6 MS. SHARKO: Please let her finish her --</p> <p>7 THE WITNESS: It's a very complicated</p> <p>8 issue.</p> <p>9 BY MS. GARBER:</p> <p>10 Q My question is --</p> <p>11 A It's not a yes-or-no answer. And IARC</p> <p>12 even says that it's not entirely clear that talc can</p> <p>13 migrate from the perineum. The data on that is</p> <p>14 weak.</p> <p>15 MS. GARBER: Objection. Motion to strike</p> <p>16 as nonresponsive.</p> <p>17 By MS. GARBER:</p> <p>18 Q Doctor --</p> <p>19 A Ma'am, I'm trying to answer you</p> <p>20 comprehensively, and I'm not going to give you a</p> <p>21 yes-or-no answer to something that's a complicated</p> <p>22 issue.</p> <p>23 Q I just need to know if, in your review of</p> <p>24 the epidemiological literature, the study authors</p> <p>25 have concluded that it's biologically plausible that</p>	<p style="text-align: right;">Page 204</p> <p>1 0o0</p> <p>2 (The deposition resumed at 2:37 p m.)</p> <p>3 0o0</p> <p>4 THE VIDEOGRAPHER: Time is now 2:36.</p> <p>5 Back on the record.</p> <p>6 BY MS. GARBER:</p> <p>7 Q Doctor, you cited to the Langseth paper</p> <p>8 2008 in your expert report; correct?</p> <p>9 A Correct.</p> <p>10 Q But you didn't cite to or address the</p> <p>11 statements that were made in that paper with regard</p> <p>12 to the issue of the biologically plausible mechanism</p> <p>13 by which talc can migrate to the ovaries, did you?</p> <p>14 MS. CURRY: Object to the form.</p> <p>15 THE WITNESS: Can you show me exactly</p> <p>16 what you're talking about.</p> <p>17 BY MS GARBER:</p> <p>18 Q I can.</p> <p>19 (C. Saenz Exhibit 12 was marked for</p> <p>20 identification.)</p> <p>21 BY MS. GARBER:</p> <p>22 Q Doctor, I've marked as Exhibit 12 the</p> <p>23 Langseth 2008 paper titled "Perineal Use of Talc and</p> <p>24 Risk of Ovarian Cancer."</p> <p>25 You have read that paper, have you not?</p>
<p style="text-align: right;">Page 203</p> <p>1 talc can migrate from the genitals to the ovaries.</p> <p>2 Have they said that in the studies? I know you</p> <p>3 disagree with it. But has that been peer reviewed</p> <p>4 and published?</p> <p>5 MS. CURRY: Object to the form.</p> <p>6 THE WITNESS: No one has concluded that</p> <p>7 because there's no data for that. They have offered</p> <p>8 it as a hypothesis, but nobody has come to that</p> <p>9 conclusion, because there's no data.</p> <p>10 BY MS. GARBER:</p> <p>11 Q The study authors have indicated that</p> <p>12 it's biologically plausible that talc can migrate</p> <p>13 from the genitals to the ovaries; true or false?</p> <p>14 MS. CURRY: Object to the form.</p> <p>15 THE WITNESS: Some of the study authors</p> <p>16 have supposed that it's possible. None of them have</p> <p>17 shown that it actually happens.</p> <p>18 MS. SHARKO: Is this a good time for a</p> <p>19 break?</p> <p>20 MS. GARBER: Do you want to take a break</p> <p>21 now?</p> <p>22 MS. CURRY: Yes, that would be great.</p> <p>23 THE VIDEOGRAPHER: The time is now 2:19.</p> <p>24 We're going off the record.</p> <p>25 (Break in the deposition taken at 2:20 p.m.)</p>	<p style="text-align: right;">Page 205</p> <p>1 A Yes, I have.</p> <p>2 Q And, Doctor, on the front page of this</p> <p>3 paper in the left-hand column about halfway down, do</p> <p>4 you see where it starts from the pathological</p> <p>5 studies?</p> <p>6 A "From pathological studies, it is known</p> <p>7 that particles and fibers that enter the body can</p> <p>8 migrate to distant organs."</p> <p>9 Q Can you keep reading?</p> <p>10 A "For instance, asbestos fibers have been</p> <p>11 found in ovaries from women exposed to asbestos.</p> <p>12 Analogously, following perineal application, talc</p> <p>13 particles can migrate from the vagina to the</p> <p>14 peritoneal cavity and ovaries."</p> <p>15 Q And you disagree with that?</p> <p>16 A I do.</p> <p>17 Q And you know that --</p> <p>18 A May I explain why, ma'am?</p> <p>19 Q No, no. It's --</p> <p>20 A Well, but you asked me a question.</p> <p>21 Q Doctor, I asked you a question, and I'll</p> <p>22 ask you another. Doctor --</p> <p>23 A That cites the Vantor article which is</p> <p>24 reference six which actually does not put talc on</p> <p>25 the perineum.</p>

Page 206	Page 208
<p>1 Q Doctor --</p> <p>2 A It's in the vagina.</p> <p>3 Q Doctor --</p> <p>4 MS. GARBER: Motion to strike as</p> <p>5 nonresponsive.</p> <p>6 BY MS. GARBER:</p> <p>7 Q Doctor, this paper is peer reviewed,</p> <p>8 correct?</p> <p>9 A Yes.</p> <p>10 Q And published?</p> <p>11 A Yes.</p> <p>12 Q Including those statements you just read.</p> <p>13 A Which are misstatements from the actual</p> <p>14 original publication.</p> <p>15 Q So the authors from IARC, some of the</p> <p>16 authors from IARC who published this paper got it</p> <p>17 wrong in your opinion?</p> <p>18 A Got it --</p> <p>19 MS. CURRY: Object to the form.</p> <p>20 THE WITNESS: Got it wrong in that</p> <p>21 statement because that's not what Ventor article</p> <p>22 shows.</p> <p>23 BY MS. GARBER:</p> <p>24 Q Okay. You also read the Ness -- you also</p> <p>25 read -- or you also reference the Ness 2000 paper in</p>	<p>1 tract inflammation such as talc can travel up an</p> <p>2 open genital tract, but with tubal ligation or</p> <p>3 hysterectomy, that pathway is cut off, thereby</p> <p>4 reducing the risk of environmentally mediated</p> <p>5 inflammation."</p> <p>6 Q Do you also disagree with this</p> <p>7 peer-review author?</p> <p>8 MS. CURRY: Object to the form.</p> <p>9 THE WITNESS: On what, on that sentence?</p> <p>10 MS. GARBER: Yes.</p> <p>11 THE WITNESS: That sentence says nothing</p> <p>12 about the perineum. So I don't disagree with that</p> <p>13 sentence because it could be something that's in the</p> <p>14 vagina.</p> <p>15 BY MS. GARBER:</p> <p>16 Q Okay. So is it your opinion that talc</p> <p>17 can migrate from the vagina to the ovaries, but when</p> <p>18 it's placed at the perineum, it cannot travel</p> <p>19 through the perineum into the vagina up the female</p> <p>20 tract to the ovaries?</p> <p>21 MS. CURRY: Object to the form.</p> <p>22 THE WITNESS: So my opinion is that</p> <p>23 there's never been a study that's looked at the</p> <p>24 travel of particulate matter from the perineum to</p> <p>25 the ovaries.</p>
Page 207	Page 209
<p>1 your expert report; did you not?</p> <p>2 A Yes, I do.</p> <p>3 Q When I say reference, I mean it's on your</p> <p>4 reference list; correct?</p> <p>5 A And I cite it in my paper.</p> <p>6 (C. Saenz Exhibit 13 was marked for</p> <p>7 identification.)</p> <p>8 BY MS. GARBER:</p> <p>9 Q I will hand you that paper. I've marked</p> <p>10 that as Exhibit 13.</p> <p>11 MS. SHARKO: What is Exhibit 13?</p> <p>12 MS. GARBER: The paper is titled "Factors</p> <p>13 Related to Inflammation of Ovarian Epithelium and</p> <p>14 Risk of Ovarian Cancer."</p> <p>15 BY MS. GARBER:</p> <p>16 Q Did I read that correctly?</p> <p>17 A Yes.</p> <p>18 Q Doctor, if you turn over to page 116, in</p> <p>19 the left-hand column, first full paragraph, could</p> <p>20 you read, could you read for me the last sentence.</p> <p>21 A I'm sorry, where?</p> <p>22 Q Left-hand column, first full paragraph --</p> <p>23 A Yes.</p> <p>24 Q -- last sentence.</p> <p>25 A "Substances that may cause lower genital</p>	<p>1 But when we're talking about biologic</p> <p>2 plausibility, there have been studies that have</p> <p>3 shown that some particulate matter placed into the</p> <p>4 vagina under certain experimental conditions can</p> <p>5 migrate to the ovaries.</p> <p>6 BY MS. GARBER:</p> <p>7 Q So is it your opinion that talc can</p> <p>8 migrate from the vagina up to the ovaries?</p> <p>9 A I don't know one way or another, but I do</p> <p>10 think that in terms of biologic plausibility, there</p> <p>11 is some data that there can be particulate matter</p> <p>12 that can make it to the ovaries, but I don't</p> <p>13 actually know one way or another if talc can do</p> <p>14 that.</p> <p>15 Q Does the literature support a</p> <p>16 biologically plausible mechanism that talc once in</p> <p>17 the vagina can reach the fallopian tubes and</p> <p>18 ovaries?</p> <p>19 MS. CURRY: Object to the form.</p> <p>20 THE WITNESS: I would say only under</p> <p>21 certain controlled situations such as the literature</p> <p>22 that I cited in my report where a slurry of</p> <p>23 particles, be they carbon particles or albumin</p> <p>24 microspheres were placed into the posterior vagina.</p> <p>25 The women were placed into Trendelenburg.</p>

<p style="text-align: right;">Page 210</p> <p>1 In the Egli study, they were given 2 oxytocin injections to incite uterine contractions, 3 so under those particular experimental 4 circumstances, there has been demonstration of 5 particulate matter in a slurry making it to the 6 ovaries. But outside of that context, there is no 7 literature. 8 BY MS. GARBER: 9 Q So those data don't have -- cannot be 10 properly extrapolated to the human experience in 11 your opinion? 12 MS. CURRY: Object to the form. 13 THE WITNESS: What human experience? 14 BY MS. GARBER: 15 Q Well, if talc is going to migrate from 16 the vagina to the ovaries, does a woman need to be 17 in Trendelenburg position? 18 MS. CURRY: Object to the form. 19 THE WITNESS: So there's no data without 20 that, for any particulate matter, so I can only 21 speak to what has actually been published in the 22 peer-reviewed literature, and those are the 23 experimental conditions under which particulate 24 matter has been shown to be found in the ovaries 25 after placement in the vagina.</p>	<p style="text-align: right;">Page 212</p> <p>1 Q You didn't think you wanted to go look at 2 that study or the FDA's banned and figure out why? 3 A No. 4 MS. CURRY: Object to the form. 5 BY MS. GARBER: 6 Q Weren't curious? 7 A No, ma'am, because again it's not 8 perineal application. 9 Q Okay. So I think I understand your 10 opinions. If talc were in the vagina and the woman 11 was under the circumstances of exogenous oxytocin in 12 a Trendelenburg position, it may be the case that 13 talc could get there. 14 Is that the limitations of your opinion? 15 MS. CURRY: Object to the form. 16 THE WITNESS: So when we're talking about 17 biologic plausibility -- 18 MS. CURRY: I'm sorry, it's highly 19 distracting, Ms. Thompson, when you're making 20 gestures and faces and speaking to other co-counsel 21 when a question is pending and the witness is trying 22 to focus and -- 23 MS. THOMPSON: Okay, I apologize. I 24 didn't realize that was -- could be overheard. At 25 least I wasn't laughing.</p>
<p style="text-align: right;">Page 211</p> <p>1 BY MS. GARBER: 2 Q Have you read the Sjosten paper? 3 A The -- I'm sorry, which one? 4 Q S-J-O-S-T-E-N, with regard to starch 5 particulate on gloves following a vaginal 6 examination? 7 A No, I've seen that referenced in some of 8 the expert reports, but that's a different 9 circumstance where my understanding is that gloves 10 were used for a pelvic exam and then they looked 11 for, I believe it was, cornstarch. 12 Q You understand that the FDA has banned 13 powdered gloves based on properties of inflammation 14 and toxicity to the female genital tract following 15 exam. You're aware of those data, aren't you? 16 MS. CURRY: Object to the form. 17 THE WITNESS: So I've not seen the FDA 18 report. I don't know that it was actually toxicity, 19 the word that you've chosen to use. I do know that 20 we no longer have powder on surgical gloves. 21 BY MS. GARBER: 22 Q I asked you about that in your deposition 23 before. Do you remember that? You hadn't seen 24 those? Don't remember that? 25 A Sounds like I'm still answering the same.</p>	<p style="text-align: right;">Page 213</p> <p>1 MS. CURRY: Smirking is very similar, but 2 in any event, it's very distracting. 3 THE WITNESS: When we're talking about 4 biologic plausibility, I would apply the science 5 that is known in terms of trying to demonstrate 6 whether or not there is biologic plausibility. And 7 the only studies that exist in humans are studies 8 where the particulate matter arises in the vagina 9 under those circumstances. 10 So in that circumstance, because of that, 11 I cannot say that talc does get to the ovaries that 12 way, but I would say that it's biologically 13 plausible in those circumstances. 14 BY MS. GARBER: 15 Q You haven't seen the Zervomanolakis paper 16 on -- with regard to mechanisms by which particulate 17 can travel, have you? 18 MS. CURRY: Object to the form. 19 THE WITNESS: From where to where? 20 BY MS. GARBER: 21 Q Are you aware of that? It's not a paper 22 that you've cited. Are you aware of that paper by 23 study author? 24 A No, ma'am. 25 Q Okay. We've already established, you</p>

<p style="text-align: right;">Page 214</p> <p>1 haven't seen the Sjosten paper; that's correct?</p> <p>2 A The paper --</p> <p>3 MS. CURRY: Object to the form.</p> <p>4 THE WITNESS: -- itself, no, but I've</p> <p>5 seen where it's been referenced, and I believe I</p> <p>6 understand the crux of that study.</p> <p>7 BY MS. GARBER:</p> <p>8 Q Have you seen the Koontz paper? Do you</p> <p>9 know that paper?</p> <p>10 A No, ma'am.</p> <p>11 Q Have you looked at Ventor 1981, ma'am?</p> <p>12 A Yes, ma'am, it's on my reference list.</p> <p>13 Q Have you seen Whittemore, 1988, what that</p> <p>14 author says about migration?</p> <p>15 A Yes, ma'am, it's on my reference list.</p> <p>16 Q Okay. All right. So Dr. Ness concludes</p> <p>17 in her 2000 paper that the female genital tract is</p> <p>18 open; correct?</p> <p>19 A What page are we on?</p> <p>20 Q On the last page that I just had you</p> <p>21 read, 116.</p> <p>22 A Where are we, ma'am?</p> <p>23 Q At the top of the paragraph you just</p> <p>24 read. Beginning with the sentence, "Substances."</p> <p>25 A Right, I disagree with her, ma'am, and</p>	<p style="text-align: right;">Page 216</p> <p>1 BY MS. GARBER:</p> <p>2 Q Let's look at your testimony. It's now</p> <p>3 your opinion that it's not an open conduit --</p> <p>4 A No.</p> <p>5 Q -- the female genital tract; right?</p> <p>6 MS. CURRY: Object to the form.</p> <p>7 THE WITNESS: Not from the perineum to</p> <p>8 the ovaries.</p> <p>9 BY MS. GARBER:</p> <p>10 Q That's not what your report says, does</p> <p>11 it? Let's go to what your report says.</p> <p>12 At the bottom of page 17, your report</p> <p>13 indicates, "But the vagina is not the perineum and</p> <p>14 the female genital tract is not an open conduit,</p> <p>15 despite Drs. Clark, Pearson, and Smith-Bindman's</p> <p>16 contrary contentions in their depositions?"</p> <p>17 A Exactly.</p> <p>18 Q So it's your opinion that the female</p> <p>19 genital tract is not an open system or tract;</p> <p>20 correct?</p> <p>21 A From the --</p> <p>22 MS. CURRY: Object to the form.</p> <p>23 THE WITNESS: -- outside, from the</p> <p>24 perineum, which is very different than from the</p> <p>25 vagina.</p>
<p style="text-align: right;">Page 215</p> <p>1 she also doesn't cite a single reference for that</p> <p>2 supposition.</p> <p>3 Q Did you cite a single reference when you</p> <p>4 said the female genital tract was closed?</p> <p>5 MS. CURRY: Object to the form.</p> <p>6 THE WITNESS: I talk about the female</p> <p>7 anatomy, ma'am.</p> <p>8 BY MS. GARBER:</p> <p>9 Q Did you cite a single reference when you</p> <p>10 said the female genital tract is not an open</p> <p>11 conduit?</p> <p>12 A It's the anatomy. I'm a gynecologic</p> <p>13 oncologist. I understand the anatomy.</p> <p>14 Q So that's your opinion, that's Cheryl</p> <p>15 Saenz's opinion?</p> <p>16 A No.</p> <p>17 MS. CURRY: Object to the form.</p> <p>18 THE WITNESS: It's the female anatomy.</p> <p>19 BY MS. GARBER:</p> <p>20 Q Doctor, when I took your deposition, did</p> <p>21 you tell me that there was an open pathway --</p> <p>22 MS. CURRY: Object to the form.</p> <p>23 MS. GARBER: -- in the female genital</p> <p>24 tract?</p> <p>25 THE WITNESS: From where to where?</p>	<p style="text-align: right;">Page 217</p> <p>1 BY MS. GARBER:</p> <p>2 Q Is it an open system once you get into</p> <p>3 the vagina to the ovaries?</p> <p>4 A There is a way that you can pass up</p> <p>5 through the cervix once something is in the vagina.</p> <p>6 But as an external genitalia stands in a woman, it's</p> <p>7 not an open pathway.</p> <p>8 This is why we need to put a speculum in</p> <p>9 somebody's vagina in order to see into the vagina.</p> <p>10 You can't see into the vagina just from looking at</p> <p>11 the perineum. You have to separate the labia</p> <p>12 majora, minora, you have to put in a speculum, and</p> <p>13 you have to open it. It's not wide open from the</p> <p>14 external genitalia to the ovaries.</p> <p>15 Q Doctor, I'm going to hand you your</p> <p>16 deposition testimony from the Echeverria case, and I</p> <p>17 will show it to you. But the question I asked you</p> <p>18 is, is the female genital tract an open pathway from</p> <p>19 the vagina to the peritoneal space.</p> <p>20 And your answer was: "In a woman that</p> <p>21 has not had a hysterectomy or a tubal ligation,</p> <p>22 there's a pathway of ascension."</p> <p>23 Is that still your opinion, Doctor?</p> <p>24 A Yeah, that's no different than what I</p> <p>25 just said to you.</p>

<p style="text-align: right;">Page 218</p> <p>1 Q Okay.</p> <p>2 A May I see that back, please, ma'am? I</p> <p>3 just want to make sure --</p> <p>4 Q Of course.</p> <p>5 A -- you're reading it accurately. Thank</p> <p>6 you. Yes, ma'am. Thank you.</p> <p>7 Q Doctor, if it's an open pathway, then why</p> <p>8 at the bottom of 18 in your expert report do you</p> <p>9 spend a half a page talking about the barriers to</p> <p>10 ascension of that open female tract?</p> <p>11 MS. CURRY: Object to the form.</p> <p>12 THE WITNESS: Because that's the female</p> <p>13 anatomy. That would be the challenges that any</p> <p>14 particular matter would face in order to ascend</p> <p>15 through retrograde migration. And what we're</p> <p>16 talking about in this particular matter is the</p> <p>17 perineal application of talc which is not the</p> <p>18 vagina.</p> <p>19 BY MS. GARBER:</p> <p>20 Q So it's your opinion that particulate</p> <p>21 that sits on the perineum has no opportunity to get</p> <p>22 inside the vagina.</p> <p>23 A It's my opinion that there's never been</p> <p>24 anything that has been published in the</p> <p>25 peer-reviewed literature that shows that something</p>	<p style="text-align: right;">Page 220</p> <p>1 MS. CURRY: Object to the form.</p> <p>2 THE WITNESS: I don't know how somebody</p> <p>3 would wipe in order for your possibility to exist.</p> <p>4 That would be mean that you're actually putting the</p> <p>5 toilet paper into your vagina which would be a very</p> <p>6 different scenario than perineal application of</p> <p>7 talc.</p> <p>8 BY MS. GARBER:</p> <p>9 Q Would it not be an opportunity for talc</p> <p>10 to get inside the vagina by way of exercise and</p> <p>11 movement?</p> <p>12 A I do not --</p> <p>13 Q Moving of the tissues?</p> <p>14 A No.</p> <p>15 MS. CURRY: Object to the form.</p> <p>16 THE WITNESS: That's not how the female</p> <p>17 anatomy lays and opposes upon itself. So no.</p> <p>18 BY MS. GARBER:</p> <p>19 Q So it's your opinion and you're going to</p> <p>20 tell this court that what gets put on the outside of</p> <p>21 the female genital tract on the perineum has zero</p> <p>22 opportunity to go into the vaginal vault, that can't</p> <p>23 happen, because that study hasn't been done?</p> <p>24 MS. CURRY: Object to the form.</p> <p>25 THE WITNESS: I'm not aware of any study</p>
<p style="text-align: right;">Page 219</p> <p>1 can migrate from the perineum to the ovaries.</p> <p>2 Q That study would never be approved</p> <p>3 because it's ridiculous; isn't that true?</p> <p>4 MS. CURRY: Object to the form.</p> <p>5 Argumentative.</p> <p>6 THE WITNESS: Why would that be</p> <p>7 ridiculous?</p> <p>8 BY MS. GARBER:</p> <p>9 Q Because of course something on the</p> <p>10 perineum is going to get inside the vagina. What</p> <p>11 about the issue of sexual intercourse? Are you</p> <p>12 saying that sexual intercourse doesn't drive what's</p> <p>13 on the outside on the inside?</p> <p>14 MS. CURRY: Object to the form.</p> <p>15 BY MS. GARBER:</p> <p>16 Q Is that not a possibility, Doctor?</p> <p>17 MS. CURRY: Object to the form.</p> <p>18 THE WITNESS: There's no data to support</p> <p>19 your opinion, ma'am.</p> <p>20 BY MS. GARBER:</p> <p>21 Q Is there -- is the fact that a woman who</p> <p>22 applies genital talc to her perineum and then wipes,</p> <p>23 using the bathroom, that would not be an opportunity</p> <p>24 for talc to go inside the vaginal wall? That would</p> <p>25 be an impossibility?</p>	<p style="text-align: right;">Page 221</p> <p>1 that has every documented the migration of any</p> <p>2 particulate matter from the perineum into the vagina</p> <p>3 and then to the ovaries, not a single one.</p> <p>4 BY MS. GARBER:</p> <p>5 Q You know that your obligations under ACOG</p> <p>6 are you're only able to testify as to what you know</p> <p>7 could be peer reviewed. Is it your testimony that</p> <p>8 you would put up for peer review a statement like</p> <p>9 that, that what is on the perineum can't possibly</p> <p>10 get inside the vaginal vault?</p> <p>11 Would you submit that for peer review,</p> <p>12 Doctor?</p> <p>13 MS. CURRY: Object to the form.</p> <p>14 THE WITNESS: It's not a peer-reviewed</p> <p>15 study, ma'am. I'm making a statement very</p> <p>16 consistent with what ACOG requires me to do, which</p> <p>17 is to use peer-reviewed literature to render my</p> <p>18 opinions.</p> <p>19 And there is no peer-reviewed literature</p> <p>20 to support what you're contending. So very</p> <p>21 consistent with ACOG guidelines, I'm not giving an</p> <p>22 opinion to something that there is no data for.</p> <p>23 ///</p> <p>24 ///</p> <p>25 ///</p>

<p style="text-align: right;">Page 222</p> <p>1 MS. GARBER: Let's actually look at what 2 ACOG says. I'm going to mark as -- I'm so sorry, 3 Ms. Curry, I only have one copy of this. 4 (C. Saenz Exhibit 14 was marked for 5 identification.) 6 BY MS. GARBER: 7 Q Doctor, this is an ACOG committee opinion 8 document, and if I could have you turn to -- it's 9 titled "Expert Testimony" and it talks about expert 10 testimony. If I could have you turn to page two of 11 three of this document. 12 MS. SHARKO: What exhibit number is this, 13 ma'am? 14 MS. GARBER: I'm sorry. 14. 15 BY MS. GARBER: 16 Q Doctor, can you turn, please, to page two 17 of three, under the numbered principles that are 18 offered as guidelines for the physician who assumes 19 the role as an expert witness. 20 Do you see where I am? 21 A Yes. 22 Q Number six says, "The physician must be 23 prepared to have the testimony given in any judicial 24 proceeding subjected to peer review by an 25 institution or professional organization to which he</p>	<p style="text-align: right;">Page 224</p> <p>1 talc from the perineum to the ovary, the migration 2 of talc from the perineum to the ovary, is 3 indisputable. You cited that in your expert report, 4 didn't you? 5 A I did. 6 Q So let's look at that. 7 (C. Saenz Exhibit 15 was marked for 8 identification.) 9 BY MS. GARBER: 10 Q I will mark as Exhibit 15 a letter which 11 you have referenced in your reference list in your 12 expert report; correct? 13 A Yes. 14 Q It's dated April 1st, 2014. It's sent 15 from the FDA to a Samuel Epstein, MD; correct? 16 A Yes. 17 Q And, Doctor, you have read this letter, 18 haven't you? 19 A Yes. 20 Q You reference it under the migration 21 section of your expert report? 22 A Yes. 23 Q In fact, you say, at page 17, "And even 24 the USFDA administration have stated, quote, "While 25 there exists no direct proof of talc in ovarian</p>
<p style="text-align: right;">Page 223</p> <p>1 or she belongs." 2 Did I read that correctly? 3 A Yes. 4 Q Would you be willing to have that 5 statement, that particulate that is sitting on the 6 perineum can't possibly get into the vaginal vault? 7 Would you be willing to have that expert opinion 8 subjected to peer review? 9 A So first of all, I think you're 10 misquoting what I said. What I said, and I would be 11 more than happy to have subject to peer review, is 12 that I'm unaware of any literature that has 13 demonstrated the migration of something from outside 14 the perineum into the vagina and to the ovaries. I 15 would be very, very proud and supportive of that 16 being subject to peer review. 17 Q There's zero literature that has said 18 that talc can get from the perineum to the ovary, 19 zero literature, none. 20 MS. CURRY: Object to the form. 21 THE WITNESS: Zero scientific literature 22 to support that contention. There is no experiment 23 that's ever been done that has showed that. 24 BY MS. GARBER: 25 Q Are you aware that the FDA has said that</p>	<p style="text-align: right;">Page 225</p> <p>1 carcinogenesis, the potential for particulates to 2 migrate from the perineum to the vagina to the 3 peritoneal cavity is indisputable." 4 Then the cite to this Exhibit 15; 5 correct? That's what your expert report says? 6 A That is what my expert report says. 7 Q In fact, let's turn to what that says and 8 where. At page five, the middle of the page, the 9 letter actually indicates the same. It's a direct 10 quote. "While there exists no direct proof of talc 11 in ovarian carcinogenesis, the potential for 12 particulates to migrate from the perineum to the 13 vagina" -- 14 A "And the vagina" -- or "and vagina." 15 Q -- "from the perineum and the vagina to 16 the peritoneal cavity is indisputable." 17 FDA says the fact that it can go from the 18 perineum to the peritoneal cavity is indisputable. 19 Correct? 20 A That's what the FDA says. 21 Q But you disagree with the FDA. 22 A I completely disagree with the FDA, on 23 that statement. 24 MS. SHARKO: I see you laughing, 25 Ms. Thompson.</p>

Cheryl Saenz, M.D.

<p style="text-align: right;">Page 226</p> <p>1 MS. THOMPSON: I didn't laugh. I smiled 2 at Ms. Garber. 3 MS. SHARKO: I think that was a laugh. 4 MS. THOMPSON: We'll let the -- 5 MS. SHARKO: Let the jury decide. 6 MS. THOMPSON: Did the tape-record -- 7 recording say. 8 THE WITNESS: Ma'am, I heard you. 9 MS. THOMPSON: Okay. We'll let the 10 record speak for itself. 11 (C. Saenz Exhibit 16 was marked for 12 identification.) 13 MS. GARBER: Dr. Saenz, I'm going to mark 14 another Exhibit 16, and I'll represent to you, this 15 is an internal document that was produced attendant 16 to this litigation by Johnson & Johnson. 17 MS. CURRY: Do you have an extra copy? 18 MS. GARBER: I do. Sorry. 19 BY MS. GARBER: 20 Q Doctor, so we can get oriented, I'll just 21 represent to you, Luzenac is one of the defendants 22 in this case. Their director of product safety, 23 Richard Zazenski is emailing Bill Ashton of J&J -- 24 or not emailing, sorry. This is a fax. The date is 25 September 30th, 2004.</p>	<p style="text-align: right;">Page 228</p> <p>1 earlier, which you said you had not seen. And the 2 Sjosten paper that is included in this facsimile is 3 titled "Retrograde Migration of Glove Powder in the 4 Human Female" -- "in the Human Female Genital 5 Tract." 6 Did I read that correctly? 7 A Yes. 8 Q You've not seen that study? 9 MS. CURRY: Object to the form. 10 THE WITNESS: I've only seen references 11 to the study. 12 BY MS. GARBER: 13 Q Here there is a fax from Luzenac to Bill 14 Ashton, saying that the study provides compelling 15 evidence of the migration hypothesis. Do you agree? 16 A No. 17 Q You don't? 18 A No. 19 Q You don't agree with the data or you 20 don't agree that that's what that fax says? 21 A The fax -- 22 MS. CURRY: Object to the form. 23 THE WITNESS: -- says that, but I don't 24 agree that the study supports that. 25 BY MS. GARBER:</p>
<p style="text-align: right;">Page 227</p> <p>1 It reads: "Bill, I came across this 2 paper this morning published in the April 2004 3 journal, Human Reproduction, an official journal of 4 the European Society for Human Reproduction and 5 Embryology. It offers some compelling evidence in 6 support of the migration hypothesis?" 7 You have not seen that before, have you? 8 A No, ma'am. 9 Q Do you remember being shown that in the 10 Echeverria trial? 11 A No, I don't remember. 12 Q Johnson & Johnson -- well, strike that. 13 It looks like defendants thought that was 14 compelling evidence that talc can migrate. Do you 15 disagree with that? 16 MS. CURRY: Object to the form. 17 THE WITNESS: So, one, I've not seen this 18 article that they're referencing to, so I don't know 19 what is being interpreted as compelling evidence and 20 not in a position to evaluate this facsimile on any 21 level. 22 MS. GARBER: Okay. 23 BY MS. GARBER: 24 Q And the article that is being discussed 25 is the Sjosten paper, which I asked you about</p>	<p style="text-align: right;">Page 229</p> <p>1 Q But you've never read the street, Doctor? 2 MS. CURRY: Object to the form. 3 THE WITNESS: Ma'am, I've just read the 4 abstract because you've handed it to me, and I've 5 also seen it referenced in the expert reports 6 before. And this is a study that's looking at women 7 undergoing pelvic exams with powder on the gloves. 8 That's not powder being applied to the perineum. 9 And as I read this abstract, that's 10 exactly what they say happened. Women underwent 11 pelvic exams. That means the fingers went into the 12 vagina. 13 BY MS. GARBER: 14 Q Do you make a habit of looking at an 15 abstract and rendering scientific opinions? I mean, 16 you looked at that abstract for about 30 seconds. 17 And then you rendered an opinion about the study. 18 Is that your custom and practice, Doctor? 19 MS. CURRY: Object to the form. 20 THE WITNESS: You asked me to comment on 21 that and whether or not I believe this facsimile 22 supported the contention of the people faxing each 23 other, ma'am. So I thought I needed to give you an 24 answer to your question so that's why I did that. 25 BY MS. GARBER:</p>

Page 230

1 Q The truth is, after Echeverria, you knew
2 full well about this internal document. It was used
3 in that litigation and the study that was behind it,
4 but you never bothered to go back and read it, did
5 you?

6 MS. CURRY: Object to the form. Would
7 you like her to review the --

8 MS. GARBER: I'll --

9 MS. CURRY: -- what's attached now?

10 MS. GARBER: I'll withdraw that question.

11 BY MS. GARBER:

12 Q If we could go -- do you still have it in
13 front of you?

14 A Which one, ma'am?

15 Q Exhibit 16.

16 A Yes.

17 Q The fax goes on to say, "Combine this
18 evidence with the theory that talc deposition in the
19 ovarian epithelium initiates epithelial
20 inflammation, which leads to epithelium
21 carcinogenesis, and you have a potential formula for
22 NTP classifying talc as a causative agent in ovarian
23 cancer."

24 Did I read that correctly?

25 A You read it correctly.

Page 231

1 Q Do you understand what the author is
2 saying there?

3 MS. CURRY: Object to the form.

4 THE WITNESS: I understand the contents
5 of his message. I don't agree with him
6 biologically.

7 BY MS. GARBER:

8 Q What do you understand he's trying to
9 convey there?

10 MS. CURRY: Object to the form.

11 THE WITNESS: That there is a theory that
12 ovarian carcinogenesis is caused by inflammation.

13 BY MS. GARBER:

14 Q In fact, they cut and paste a diagram or
15 a flow chart as to the mechanism by which that may
16 occur, don't they?

17 MS. CURRY: Object to the form.

18 THE WITNESS: I don't know.

19 BY MS. GARBER:

20 Q You don't recognize this diagram?

21 A No.

22 Q You don't remember it from the Echeverria
23 trial?

24 A No.

25 Q Let's refresh your memory. A source of

Page 232

1 that diagram comes from the Ness paper, the Ness
2 2099 paper --

3 A We're not in 2099.

4 Q I'm sorry. Did I say that?

5 A Uh-huh.

6 Q I do that all the time. Thank you.
7 1999.

8 MS. GARBER: I'll mark that as
9 Exhibit 17.

10 (C. Saenz Exhibit 17 was marked for
11 identification.)

12 BY MS. GARBER:

13 Q If you -- if you turn to page two of that
14 paper, do you see that the figure one diagram is the
15 same as appears on Exhibit 16, fax?

16 A Yes, ma'am, it looks the same.

17 Q All right. And if we look at Exhibit 17,
18 figure one indicates inflammation as a common
19 mechanism underlying ovarian cancer.

20 Do you see that?

21 A Yes, I see the wording saying that; yes.

22 Q Right. And this study was a
23 peer-reviewed, published scientific paper; correct?

24 A Well --

25 Q Exhibit 17?

Page 233

1 A I wouldn't really classify it as that,
2 because it's a review article. So it's --

3 Q Don't peer review -- or don't review
4 papers undergo the peer review process before
5 publication?

6 A Not necessarily --

7 MS. CURRY: Object to the form.

8 THE WITNESS: -- the same way. Sometimes
9 authors are invited to write a review article. So
10 it doesn't actually then go out to reviewers for
11 review.

12 So no.

13 BY MS. GARBER:

14 Q Okay. But the defendants in this case
15 thought enough of this article that they cut and
16 paste this diagram into their fax to talk about the
17 inflammation mechanism, didn't they?

18 MS. CURRY: Object to the form.

19 THE WITNESS: So I'm not in a position to
20 comment on what the actual purpose of this was back
21 in 2004. Inflammation is a hypothesis as to the
22 potential for ovarian carcinogenesis, but there is
23 not actually any mechanistic data that shows that
24 that is true.

25 So this is a hypothesis.

<p style="text-align: right;">Page 234</p> <p>1 BY MS. GARBER:</p> <p>2 Q There's no mechanistic data that supports</p> <p>3 inflammation as a mechanism that you've reviewed.</p> <p>4 MS. CURRY: Object to the form.</p> <p>5 THE WITNESS: Correct.</p> <p>6 BY MS. GARBER:</p> <p>7 Q Let's look at this figure one. At the</p> <p>8 top left, it indicates "Epithelial Inflammation</p> <p>9 Initiators." What do you understand that to mean</p> <p>10 scientifically?</p> <p>11 A I don't actually know what the author is</p> <p>12 referring to here.</p> <p>13 Q Okay.</p> <p>14 A I would have to see within the article</p> <p>15 what she's referring to here.</p> <p>16 Q Okay. Then there's a downward arrow and</p> <p>17 a positive sign there. So what do you think that</p> <p>18 means scientifically as a review of scientific</p> <p>19 literature?</p> <p>20 MS. CURRY: Object to the form.</p> <p>21 THE WITNESS: That it has a positive</p> <p>22 influence.</p> <p>23 BY MS. GARBER:</p> <p>24 Q All right. And then in that center box,</p> <p>25 there is the word "inflammation"; correct?</p>	<p style="text-align: right;">Page 236</p> <p>1 BY MS. GARBER:</p> <p>2 Q Are you aware that the Buz'Zard 2007 data</p> <p>3 showed mechanistic data supporting talc and elevated</p> <p>4 oxidative stress or reactive oxygen species?</p> <p>5 A No.</p> <p>6 MS. CURRY: Object to the form.</p> <p>7 THE WITNESS: I've not read that paper,</p> <p>8 ma'am.</p> <p>9 BY MS. GARBER:</p> <p>10 Q All right. Are you aware that the</p> <p>11 Shukla data supported an elevated cytokines after</p> <p>12 talc exposure?</p> <p>13 MS. CURRY: Object to the form.</p> <p>14 THE WITNESS: I have not read that paper,</p> <p>15 ma'am.</p> <p>16 MS. GARBER: All right.</p> <p>17 MS. SHARKO: Ms. Garber and Ms. Thompson,</p> <p>18 going forward, can you please bring copies of</p> <p>19 exhibits for all counsel. I know there's two</p> <p>20 defendants down here who aren't getting anything.</p> <p>21 You've given one copy for us. I think the case</p> <p>22 management order addresses the number of copies.</p> <p>23 MS. GARBER: Ms. Sharko, I would be happy</p> <p>24 to do that, but that was not provided to us when we</p> <p>25 defended our experts and it's a significant cost and</p>
<p style="text-align: right;">Page 235</p> <p>1 A Yes, ma'am.</p> <p>2 Q Then below that, there's a number of</p> <p>3 bullet points. One is DNA damage and repair;</p> <p>4 correct?</p> <p>5 A Correct.</p> <p>6 Q One is oxidative stress; correct?</p> <p>7 A Yes, ma'am.</p> <p>8 Q One is elevated cytokines and</p> <p>9 prostaglandins; correct?</p> <p>10 A Yes, ma'am.</p> <p>11 Q Then a downward arrow ends in the words</p> <p>12 "ovarian carcinogenesis"; correct?</p> <p>13 A Yes, ma'am.</p> <p>14 Q Are you aware that the Saed data</p> <p>15 provide -- 2019 paper provided mechanistic data</p> <p>16 supporting DNA damage?</p> <p>17 MS. CURRY: Object to the form.</p> <p>18 THE WITNESS: No, ma'am.</p> <p>19 BY MS. GARBER:</p> <p>20 Q Okay. Are you aware that the Saed data</p> <p>21 provided mechanistic data between talc and inducing</p> <p>22 oxidative stress?</p> <p>23 MS. CURRY: Object to the form.</p> <p>24 THE WITNESS: I do believe that he showed</p> <p>25 that; yes.</p>	<p style="text-align: right;">Page 237</p> <p>1 we tried to bring our own copies of things.</p> <p>2 I'll do my best in the depositions I'm</p> <p>3 taking to do that in the future.</p> <p>4 MS. SHARKO: Okay, well --</p> <p>5 MS. GARBER: Flying on an airplane is a</p> <p>6 lot of money to take multiple copies.</p> <p>7 MS. SHARKO: All right, well, I disagree</p> <p>8 with what you're saying about the other depositions,</p> <p>9 and I'll take up the violation of the order with</p> <p>10 your lead counsel.</p> <p>11 MS. GARBER: We did our best to provide</p> <p>12 copies here today. I understood that this witness</p> <p>13 would be defended by one lawyer, and I have brought</p> <p>14 copies for her.</p> <p>15 MS. SHARKO: I think my friends at the</p> <p>16 end of the table would appreciate copies.</p> <p>17 BY MS. GARBER:</p> <p>18 Q Doctor, we've now gone through a number</p> <p>19 of studies where the tract -- where the published</p> <p>20 peer-reviewed authors have stated that it's</p> <p>21 biologically plausible that talc can migrate.</p> <p>22 But is it a true statement that nowhere</p> <p>23 in the four corners of your report do you discuss or</p> <p>24 analyze those statements?</p> <p>25 MS. CURRY: Object to the form.</p>

<p style="text-align: right;">Page 238</p> <p>1 THE WITNESS: So I discuss and analyze</p> <p>2 the data that's actually on studies of migration. I</p> <p>3 don't discuss every proposal that any author may</p> <p>4 ever have made that such a supposition is true.</p> <p>5 What I discuss is the actual experiments</p> <p>6 that evaluated migration.</p> <p>7 BY MS. GARBER:</p> <p>8 Q And we've already established that you</p> <p>9 have not considered the totality of the literature</p> <p>10 in connection with the issue of whether talc can</p> <p>11 migrate; correct?</p> <p>12 MS. CURRY: Object to the form.</p> <p>13 THE WITNESS: No, I disagree with you,</p> <p>14 ma'am. Having an author put in their paper that</p> <p>15 they propose migration can exist is not a scientific</p> <p>16 evaluation of the migration theory. It's a</p> <p>17 statement. And I'm not going to put in my report</p> <p>18 statements that are not based on -- in an experiment</p> <p>19 into my report.</p> <p>20 My report contains references to Egli, it</p> <p>21 contains references to Ventor, and those authors</p> <p>22 actually published on migration. And those papers</p> <p>23 are in my report.</p> <p>24 Having Dr. Ness suggest a proposal that</p> <p>25 migration exists is not something that belongs in my</p>	<p style="text-align: right;">Page 240</p> <p>1 A It's the actual contraction mechanism of</p> <p>2 the uterus. That's, in fact, triggered by oxytocin.</p> <p>3 Q And do you have any knowledge that</p> <p>4 oxytocin can stimulate both antegrade contractions</p> <p>5 as well as retrograde contractions of the female</p> <p>6 genital tract?</p> <p>7 MS. CURRY: Object to the form.</p> <p>8 THE WITNESS: The directionality of flow</p> <p>9 can be either way.</p> <p>10 BY MS. GARBER:</p> <p>11 Q That is a biologically plausible</p> <p>12 mechanism by which particulate can move up the</p> <p>13 female genital tract; right?</p> <p>14 MS. CURRY: Object to the form.</p> <p>15 THE WITNESS: From the posterior vagina</p> <p>16 as a slurry.</p> <p>17 BY MS. GARBER:</p> <p>18 Q What happens to talc when it mixed with</p> <p>19 the vaginal fluids. Doesn't it act like a slurry?</p> <p>20 MS. CURRY: Object to the form.</p> <p>21 THE WITNESS: I don't know. I haven't</p> <p>22 seen any studies on talc mixing with vaginal fluids.</p> <p>23 BY MS. GARBER:</p> <p>24 Q Don't the authors indicate -- the study</p> <p>25 authors indicate that those studies are applicable</p>
<p style="text-align: right;">Page 239</p> <p>1 report as scientific evidence of migration.</p> <p>2 MS. GARBER: Objection. Move to strike</p> <p>3 as nonresponsive.</p> <p>4 BY MS. GARBER:</p> <p>5 Q Doctor, are you aware that the female</p> <p>6 genital tract has a mechanism by which retrograde</p> <p>7 transport of particulate can move up the female</p> <p>8 genital tract?</p> <p>9 MS. CURRY: Object to the form.</p> <p>10 THE WITNESS: From where to where?</p> <p>11 BY MS. GARBER:</p> <p>12 Q Well, let's say from the vaginal vault up</p> <p>13 to the fallopian tubes.</p> <p>14 A I'm aware of some studies that have been</p> <p>15 conducted that have demonstrated the migration of</p> <p>16 particulate matter from the posterior vaginal vault</p> <p>17 in a slurry to the fallopian tubes under certain</p> <p>18 scientific experimental conditions.</p> <p>19 Q And those are limited to the studies that</p> <p>20 you've cited in your report; correct?</p> <p>21 A Correct.</p> <p>22 Q Have you heard of a peristaltic pump with</p> <p>23 regard to the female genital tract?</p> <p>24 A I've heard that phrase used; yes.</p> <p>25 Q Do you know what that is?</p>	<p style="text-align: right;">Page 241</p> <p>1 to talc?</p> <p>2 A Which study authors?</p> <p>3 MS. CURRY: Object to the form.</p> <p>4 BY MS. GARBER:</p> <p>5 Q The published studies that cite to that</p> <p>6 there's a biologically plausible mechanism, that</p> <p>7 cite Egli and Ventor and some of the studies that</p> <p>8 you have cited, that it's biologically plausible</p> <p>9 that talc can migrate from the genitals to the</p> <p>10 ovaries.</p> <p>11 A So --</p> <p>12 MS. CURRY: Object to the form.</p> <p>13 THE WITNESS: -- the authors don't</p> <p>14 actually make that leap. They do say those studies</p> <p>15 support the migration, but they're misquoting Egli</p> <p>16 and Ventor because Egli and Ventor actually have the</p> <p>17 slurry start in the posterior vagina, not on the</p> <p>18 peritoneum.</p> <p>19 BY MS. GARBER:</p> <p>20 Q If I were to put any study in front of</p> <p>21 you that said talc can migrate and it was a study</p> <p>22 author that studied genital talc in ovarian cancer,</p> <p>23 any study author who was peer reviewed and published</p> <p>24 who said that is a biologically plausible mechanism,</p> <p>25 you would say they're wrong?</p>

<p style="text-align: right;">Page 242</p> <p>1 MS. CURRY: Object to the form.</p> <p>2 THE WITNESS: I would say to you, show me</p> <p>3 the science, show me the experiment that they are</p> <p>4 making this statement from. That's what I would say</p> <p>5 to you.</p> <p>6 BY MS. GARBER:</p> <p>7 Q Have you acknowledged in your expert</p> <p>8 report any of the published authors' statements with</p> <p>9 regard to the biologically plausible mechanisms for</p> <p>10 talcum powder products' carcinogenicity and chronic</p> <p>11 inflammation?</p> <p>12 MS. CURRY: Object to the form.</p> <p>13 THE WITNESS: So I don't exactly know</p> <p>14 what you're referencing to. I have done an analysis</p> <p>15 in my report as to whether or not there's evidence</p> <p>16 of chronic inflammation with talc being found in the</p> <p>17 ovaries.</p> <p>18 I've also done an analysis in my report</p> <p>19 as to whether or not we see evidence of foreign body</p> <p>20 granulomas in ovarian cancer.</p> <p>21 (C. Saenz Exhibit 18 was marked for</p> <p>22 identification.)</p> <p>23 MS. GARBER: Doctor, I'm going to mark as</p> <p>24 Exhibit 18, a document again, that I created. It is</p> <p>25 titled "Biologic Plausibility Chronic Inflammation."</p>	<p style="text-align: right;">Page 244</p> <p>1 even correspond to the methods, the data collection,</p> <p>2 and what the results were of these studies.</p> <p>3 I do believe that many of these comments</p> <p>4 most likely came from the discussion sections of</p> <p>5 these papers, and that's not scientific proof of</p> <p>6 that hypothesis.</p> <p>7 BY MS. GARBER:</p> <p>8 Q Doctor, it's your opinion that talc does</p> <p>9 not induce chronic inflammation; correct?</p> <p>10 MS. CURRY: Object to the form.</p> <p>11 THE WITNESS: In what venue?</p> <p>12 BY MS. GARBER:</p> <p>13 Q With regard to the initiation of ovarian</p> <p>14 cancer as a possible mechanism.</p> <p>15 A That's correct.</p> <p>16 Q There are a number of peer-reviewed</p> <p>17 publications that indicate otherwise; correct?</p> <p>18 MS. CURRY: Object to the form.</p> <p>19 THE WITNESS: No, ma'am. All of these</p> <p>20 are hypotheses. They're not indicating that ovarian</p> <p>21 cancer is caused by chronic inflammation or talc.</p> <p>22 They all say, basically -- I mean, right here,</p> <p>23 ma'am, your own reference that you cherry-picked,</p> <p>24 one, two, three, four, five, six, seven down. This</p> <p>25 is the Wu paper, "with previous findings and are</p>
<p style="text-align: right;">Page 243</p> <p>1 Doctor, I will represent to you that</p> <p>2 these are a listing of peer-reviewed study</p> <p>3 publications that address the issue of talc's</p> <p>4 ability to induce chronic inflammation. I'll</p> <p>5 represent that to you.</p> <p>6 MS. CURRY: I have the same objection to</p> <p>7 Exhibit 18 as I do to Exhibit 11.</p> <p>8 MS. GARBER: You may, Ms. Curry.</p> <p>9 BY MS. GARBER:</p> <p>10 Q Doctor, nowhere in the four corners of</p> <p>11 your report have you attempted to settle or respond</p> <p>12 to these statements with regard to peer-reviewed,</p> <p>13 published study authors' statements with regard to</p> <p>14 talc's induction of chronic inflammation, have you?</p> <p>15 MS. CURRY: Object to the form. If you</p> <p>16 need to review this document in full, please do so</p> <p>17 before responding, as well as other underlying</p> <p>18 documents.</p> <p>19 THE WITNESS: Well, ma'am, first I'm</p> <p>20 going to disagree with you, because not all of these</p> <p>21 are peer reviewed or published.</p> <p>22 Secondly, I'm going to disagree with you</p> <p>23 because I believe that what you've done here is</p> <p>24 cherry-picked comments that each of the authors have</p> <p>25 made from these publications and may not necessarily</p>	<p style="text-align: right;">Page 245</p> <p>1 compatible with the hypothesis."</p> <p>2 So these are not statements of fact.</p> <p>3 They are hypotheses.</p> <p>4 BY MS. GARBER:</p> <p>5 Q You understand the biologic plausibility</p> <p>6 for the mechanism does not require proof. It's only</p> <p>7 a plausible mechanism; correct?</p> <p>8 MS. CURRY: Object to the form.</p> <p>9 BY MS. GARBER:</p> <p>10 Q You understand that, don't you?</p> <p>11 A For which you need to have a scientific</p> <p>12 basis and not a single one of these statements is</p> <p>13 the scientific basis.</p> <p>14 Q Provide for me the support of that</p> <p>15 statement.</p> <p>16 A Provide for you the support?</p> <p>17 Q Yeah.</p> <p>18 A You can't just say something is so and</p> <p>19 have it be so. A hypothesis has to actually be</p> <p>20 based in scientific proof of some sort. There's no</p> <p>21 mechanistic study that shows that talc leads to</p> <p>22 ovarian carcinogenesis via chronic inflammation.</p> <p>23 Q Doctor, you understand that in a</p> <p>24 causation analysis, there is no necessity to prove</p> <p>25 mechanism of carcinogenicity; right? You understand</p>

Page 246

1 that?

2 MS. CURRY: Object to the form.

3 THE WITNESS: Ma'am, I disagree with you.

4 Biologic plausibility means that you actually have

5 to have some scientific proof that that mechanism

6 exists or makes sense. And there is no scientific

7 proof that talc leads to chronic inflammation in the

8 ovaries.

9 There's also no scientific proof that

10 chronic inflammation leads to ovarian

11 carcinogenesis.

12 BY MS. GARBER:

13 Q Provide for me the citation that supports

14 that definition of biologically plausibility.

15 A Ma'am, I can't provide for you something

16 that is saying, you can just say a hypothesis and it

17 is so. That's not what an analysis is about.

18 Biologic plausibility can be an extension whereby

19 you say, if we have seen X, Y, or Z in A, B, C, then

20 by extension, it's biologically plausible that it

21 also exists in X, Y, and Z. You can't just say we

22 have this hypothesis and so, therefore, it's so.

23 (C. Saenz Exhibit 19 was marked for

24 identification.)

25 MS. GARBER: Let's mark as Exhibit 19 a

Page 247

1 draft screening assessment from Health Canada.

2 MS. CURRY: Do you guys need to see

3 copies of these exhibits because I may have extra

4 copies of some of them if you need them.

5 MR. ANDERTON: If you have them, that

6 would be great. And I guess going forward, I would

7 tend to agree, that we're going to be at these depositions

8 and in the interest of checking them --

9 MS. GARBER: Well, then you guys are

10 going to need to let us know how many of you are

11 going to attend so that we know that --

12 MR. ANDERTON: We're here as a party, so

13 at least one for each party would be appropriate in

14 my mind.

15 MS. GARBER: Thank you.

16 MS. SHARKO: You can assume fairly that

17 you need four copies of every exhibit. That is what

18 we did.

19 BY MS. GARBER:

20 Q Doctor, if you could turn to page 18 of

21 this paper. With regard to -- or sorry, turning to

22 the middle of the document under the title, "Mode of

23 Action," it's right after the Keskin citation.

24 Do you see where I am?

25 A Yes.

Page 248

1 Q It indicates, "There is support for an

2 association of inflammation and increased risk of

3 ovarian cancer," and it cites to the National

4 Academy of Sciences and Engineering, 2016, and that

5 Rasmussen paper.

6 Do you disagree with that statement?

7 A So I've not read the N-A-S [sic] paper,

8 so I don't actually know if the authors are quoting

9 it correctly or not.

10 And which of the Rasmussen -- oh, it's

11 only the published one. I actually have read the

12 Rasmussen paper. And the only positive finding in

13 that study for an inflammatory process which would

14 be pelvic inflammatory disease was found with an

15 association of borderline tumors, and that was only

16 after, I believe, the second episode of pelvic

17 inflammatory disease.

18 So I can't comment on the reference of

19 the N-A-S paper and I think that the statement that

20 there is support for an association of inflammation

21 and increased risk of ovarian cancer is really kind

22 of an overbroad generalization because it really

23 only did pertain to borderline tumors.

24 Q That's a long way of saying no?

25 MS. CURRY: Object to the form.

Page 249

1 THE WITNESS: Ma'am, I'm sorry. I'm just

2 trying to be complete for you so you understand why

3 I say what I'm saying.

4 BY MS. GARBER:

5 Q Did you read the Trabert paper, 2014,

6 titled "Pre-diagnostic Serum Levels of Inflammation

7 Markers and the Risk of Ovarian Cancer in the

8 Prostate, Lung, Colorectal, and Ovarian Cancer,

9 P-L-C-O, Screening Trial"?

10 A I don't think it's in my report, but I

11 might have read it somewhere around the course of my

12 career.

13 Q I didn't see it in your citations.

14 A But I do think that -- I know I've read

15 various publications from the P-L-C-O trial --

16 sorry, the P-L-C-O clinical trials. So I don't know

17 if I've, off the top of my head, read that

18 particular one. I'd be happy to take a look at it

19 for you.

20 But the --

21 Q I --

22 A -- P-L-C-O trials are something that the

23 GYN oncology community has paid attention to.

24 Q So I just want to read for you a

25 statement. It says "Research Highlights" at page

Page 250

1 13. It says, "Our study provides additional
2 evidence that" --
3 MS. CURRY: I'm sorry, do you have a copy
4 of that?
5 MS. GARBER: I don't.
6 BY MS. GARBER:
7 Q "Our study provides additional evidence
8 that inflammation plays an important role in ovarian
9 carcinogenesis." If that's what it says, do you
10 disagree with that?
11 A Why don't we just --
12 MS. CURRY: Object to the form. Do you a
13 copy so we can look at it?
14 MS. GARBER: You don't have a copy?
15 MS. CURRY: No, can we take a look at
16 what you're quoting?
17 BY MS. GARBER:
18 Q If that's what it says, do you disagree
19 with that?
20 A I can't comment on that one way or
21 another because I don't know what they're referring
22 to as inflammation. If it's something such as an
23 elevated CA 125 versus looking at the actually
24 ovaries.
25 So without looking at the study, I can't

Page 251

1 comment on that statement.
2 Q What is Interleukin 8?
3 A Interleukin 8, it's an inflammatory
4 marker.
5 Q Is it -- so it's associated with
6 inflammation?
7 MS. CURRY: Object to the form.
8 THE WITNESS: It can be.
9 BY MS. GARBER:
10 Q Has it been tied to risk of ovarian
11 cancer or a pathway of developing ovarian cancer?
12 MS. CURRY: Object to the form.
13 THE WITNESS: I'm sure there are some
14 publications that have shown Interleukin 8 levels
15 are elevated, but where along the pathway of
16 carcinogenesis, off the top of my head, I don't
17 really know how that would relate.
18 BY MS. GARBER:
19 Q You reference the Gates 2018 study in
20 your reference list.
21 A No, ma'am, there's no Gates 2018 study.
22 Q I'm sorry, 2008; correct?
23 A Yes, ma'am.
24 ///
25 ///

Page 252

1 MS. GARBER: I'll mark that study as
2 Exhibit 20.
3 (C. Saenz Exhibit 20 was marked for
4 identification.)
5 BY MS. GARBER:
6 Q Doctor, if I could call your attention to
7 page eight, the first full paragraph about halfway
8 down, the sentence begins, "Talc particles."
9 Do you see that?
10 A I'm sorry, which paragraph?
11 Q The first full paragraph.
12 A Oh. Halfway down. Okay.
13 Q Could you read what those two sentences
14 until you reach the note -- I'm sorry, the citation
15 11.
16 A "Talc particles can induce an
17 inflammatory response in vivo, which may be
18 important in ovarian cancer."
19 Q Keep going. One more sentence.
20 A Hold on one second. "Normal ovarian
21 cells treated with talc are more likely to undergo
22 self-proliferation and neoplastic trans -- whoops,
23 neoplastic transformation and cellular generation of
24 reactive oxygen species increasing with increasing
25 exposure to talc."

Page 253

1 Q Do you disagree with those sentences?
2 A No.
3 Q Okay. You also cited to the Mills 2008,
4 study; correct?
5 MS. CURRY: Object to the form.
6 I don't believe --
7 MS. GARBER: I'm sorry, 2004. That's
8 what I do when I get tired. I get my numbers all
9 mixed up. You also -- I'll start over.
10 BY MS. GARBER:
11 Q You also reference the Mills 2004 study
12 in your expert report references; correct?
13 A Yes.
14 (C. Saenz Exhibit 21 was marked for
15 identification.)
16 BY MS. GARBER:
17 Q If you could turn to page 458 of this
18 paper.
19 A That's the first page.
20 Q Okay. This is a peer-reviewed
21 publication; correct?
22 A Yes.
23 Q This concerned perineal talc exposure and
24 epithelial ovarian cancer risk; correct?
25 A Yes.

<p style="text-align: right;">Page 254</p> <p>1 Q And with regard to the issue of migration 2 in the first full paragraph, it reads: "In animal 3 studies, talc and other substances have been 4 demonstrated to migrate from the vagina through the 5 peritoneal cavity to the ovaries." 6 Did I read that correctly? 7 A Yes. 8 Q And this is in your -- another 9 peer-reviewed paper where the authors have stated 10 that; correct? 11 A Ma'am, that's the -- 12 MS. CURRY: Object to the form. 13 THE WITNESS: -- introduction. That's 14 not anything that they're proving in this paper. 15 BY MS. GARBER: 16 Q And with regard to the issue of 17 inflammation, the authors state, and it has been 18 peer reviewed, "Collectively, these studies point to 19 a possible etiologic role of talc in ovarian cancer, 20 via inflammation process at the site of the ovarian 21 epithelium." 22 Did I read that correctly? 23 MS. CURRY: Inflammatory process. 24 BY MS. GARBER: 25 Q I'm sorry. "Collectively, these studies</p>	<p style="text-align: right;">Page 256</p> <p>1 It's talking about hypotheses. 2 BY MS. GARBER: 3 Q Doctor, at page 20 of your expert report, 4 you indicate that "There is no data to support that 5 inflammation is the underlying -- "There is no data 6 to support that inflammation is underlying the" -- 7 A I'm sorry, ma'am, where are we? 8 Q Under the summary. 9 A Okay. 10 Q I'll start again. In your expert report 11 at page 20, you indicate, "There is no data to 12 support inflammation is the underlying" -- "is 13 underlying the" -- 14 A Wait, I'm sorry. I don't see where you 15 are. 16 MS. CURRY: I don't either. 17 BY MS. GARBER: 18 Q Doctor, under "Summary" -- 19 A Yes, ma'am. 20 Q -- at the very end, do you see where I 21 am? 22 MS. CURRY: You're reading the last half 23 of the sentence. 24 THE WITNESS: You're starting in the 25 middle of a sentence.</p>
<p style="text-align: right;">Page 255</p> <p>1 point to a possible etiologic role of talc in 2 ovarian cancer via an inflammatory process at the 3 site of the ovarian epithelium." 4 Did I now read that correctly? 5 A You read it correctly, but the paper that 6 they're citing there and referencing is the Ness 7 2000 paper, which actually was about hypotheses of 8 ovarian cancer in mutagenesis and was not a 9 mechanistic paper. 10 So it's not describing actually the 11 inflammation. It's theorizing. 12 And, again, this is the introduction. 13 It's not anything that's being proven in this paper. 14 Q This has been peer reviewed and 15 published, so it's undergone a peer-review process 16 that your opinions have not; true? 17 MS. CURRY: Object to the form. 18 THE WITNESS: Ma'am, the introduction is 19 not the result of the study. And a statement that 20 the author makes doesn't make it so, particularly if 21 it's in the introduction or the discussion section. 22 There's nothing in the results of this 23 paper that supports that, and in fact, the paper 24 that they cite for that statement is Ness 2000, 25 which actually doesn't look at inflammation per se.</p>	<p style="text-align: right;">Page 257</p> <p>1 BY MS. GARBER: 2 Q Okay. All right. I'll read the whole 3 sentence. "The clinical and epidemiologic data" -- 4 so we'll start there. 5 What does "clinical data" mean? 6 A Patients, ovaries themselves, looking for 7 foreign body granulomas, associations of pelvic 8 inflammatory disease with the development of ovarian 9 cancer. 10 Q What you've seen with your eyes? 11 A What I've seen with my eyes, but also the 12 literature on PID that we discussed earlier, the 13 Rasmussen study. 14 Q Okay. So the clinical an epidemiological 15 data, and there you mean the data that we've been 16 going through, the published, peer-reviewed 17 epidemiological data with regard to genital talc and 18 risk of ovarian cancer, correct? 19 A Yes, ma'am. 20 Q You indicate, "do not support the 21 hypothesis that talc causes ovarian cancer through 22 induction of chronic inflammatory process, primarily 23 because there's no data to support that inflammation 24 is underlying the malignant transformation of the 25 ovarian epithelium at all."</p>

<p style="text-align: right;">Page 258</p> <p>1 Did I read that correctly?</p> <p>2 A Yes.</p> <p>3 Q And you have made that statement without</p> <p>4 reviewing the totality of the literature with regard</p> <p>5 to mechanisms of carcinogenicity; correct?</p> <p>6 MS. CURRY: Object to the form.</p> <p>7 THE WITNESS: No, ma'am. I've reviewed</p> <p>8 the data on mechanisms of carcinogenicity and</p> <p>9 ovarian cancer and I've also reviewed the clinical</p> <p>10 data, which we talked about, and I've also reviewed</p> <p>11 the pathologic data and the epidemiologic data.</p> <p>12 BY MS. GARBER:</p> <p>13 Q Which pathologic data did you review?</p> <p>14 A Whenever we operate on patients, we don't</p> <p>15 see evidence of foreign body granulomas. We don't</p> <p>16 see evidence of chronic inflammation. From a</p> <p>17 pathologic standpoint, there's no evidence of</p> <p>18 inflammation underlying the development of ovarian</p> <p>19 cancer.</p> <p>20 Q Okay. And I'm going to get to that. I</p> <p>21 just wondered if you had seen some patient-level</p> <p>22 data in this case or something you were referencing.</p> <p>23 MS. CURRY: Object to the form.</p> <p>24 THE WITNESS: I don't know what you mean,</p> <p>25 patient --</p>	<p style="text-align: right;">Page 260</p> <p>1 for a plausible mechanism of how that happens? What</p> <p>2 would such a study do?</p> <p>3 MS. CURRY: Object to the form.</p> <p>4 THE WITNESS: It would look for malignant</p> <p>5 transformation from a normal cell.</p> <p>6 BY MS. GARBER:</p> <p>7 Q Would it also look for inflammatory</p> <p>8 factors and mechanistic data by which malignant</p> <p>9 transformation could happen?</p> <p>10 MS. CURRY: Object to the form.</p> <p>11 THE WITNESS: Only if you believed that</p> <p>12 chronic inflammation might be involved in the</p> <p>13 process of malignant transformation.</p> <p>14 BY MS. GARBER:</p> <p>15 Q Are you aware of data that chronic</p> <p>16 inflammation is associated with malignant</p> <p>17 transformation in any context?</p> <p>18 A In other tumors, yes, about not in</p> <p>19 ovarian cancer.</p> <p>20 Q Okay. Now, you also indicate in your</p> <p>21 report -- and I think we were just talking about the</p> <p>22 pathologic data. And you talk about when you've</p> <p>23 performed surgery on patients and what you've seen</p> <p>24 macroscopically; right, with your naked eye.</p> <p>25 A Also microscopically.</p>
<p style="text-align: right;">Page 259</p> <p>1 MS. GARBER: Never mind. I'll withdraw.</p> <p>2 BY MS. GARBER:</p> <p>3 Q But when you claim no epidemiologic or</p> <p>4 biologic data, as we have established over and over,</p> <p>5 you have not seen the Buz'Zard or Shukla paper;</p> <p>6 correct?</p> <p>7 A Correct. But those don't demonstrate</p> <p>8 cancer.</p> <p>9 Q They demonstrate mechanism, don't they?</p> <p>10 MS. CURRY: Object to the form.</p> <p>11 THE WITNESS: No, they demonstrate</p> <p>12 inflammatory processes. They don't demonstrate</p> <p>13 cancer.</p> <p>14 BY MS. GARBER:</p> <p>15 Q Okay. What is the purpose of a cellular</p> <p>16 study with regard to, let's say, applying talc to a</p> <p>17 given cell to assess what happens at the cellular</p> <p>18 level? What would be the purpose of doing such a</p> <p>19 study?</p> <p>20 MS. CURRY: Object to the form.</p> <p>21 THE WITNESS: It all depends on what your</p> <p>22 hypothesis is.</p> <p>23 BY MS. GARBER:</p> <p>24 Q What if your hypothesis is that talc can</p> <p>25 induce epithelium ovarian cancer and you're looking</p>	<p style="text-align: right;">Page 261</p> <p>1 Q I'm going to get there. I'm breaking it</p> <p>2 down. So you're describing what you see with your</p> <p>3 eyes, macroscopically, when you operate, and you</p> <p>4 remove their, let's say, ovaries; correct?</p> <p>5 A Their cancer?</p> <p>6 Q Uh-huh.</p> <p>7 A Yes.</p> <p>8 Q You also review their pathological --</p> <p>9 their pathology slides of the tissue that you've</p> <p>10 removed; correct?</p> <p>11 A Yes.</p> <p>12 Q And you use that as support for your</p> <p>13 opinion that talc can't induce chronic inflammation</p> <p>14 that leads to cancer, because when you look with</p> <p>15 your eyes and look under the microscope, you don't</p> <p>16 see evidence of that in the tumor?</p> <p>17 A That's some of what --</p> <p>18 MS. CURRY: Object to the form.</p> <p>19 BY MS. GARBER:</p> <p>20 Q Is that fair?</p> <p>21 A That's some of what I use to support it,</p> <p>22 I've not seen evidence of foreign body granulomas,</p> <p>23 other things that would suggest that foreign bodies</p> <p>24 are actually causing it. Yes.</p> <p>25 Q Isn't it true, though, Doctor, by the</p>

<p style="text-align: right;">Page 262</p> <p>1 time you see the cancer, the inflammatory process</p> <p>2 has already been overtaken by the tumor? You're not</p> <p>3 going to see at time of diagnosis what happened</p> <p>4 years earlier, way before the latency period as</p> <p>5 there was transformation of those normal cells into</p> <p>6 cancer cells, are you?</p> <p>7 MS. CURRY: Object to the form.</p> <p>8 THE WITNESS: I have no reason to believe</p> <p>9 that that's accurate. I think that if there was</p> <p>10 evidence of foreign body granulomas, they would</p> <p>11 still be there in the pathology that we're</p> <p>12 reviewing.</p> <p>13 BY MS. GARBER:</p> <p>14 Q Is it a true statement that today, when</p> <p>15 you're looking at, let's say, ovarian tissue, you</p> <p>16 have no way of seeing cancerous transformation when</p> <p>17 it occurred years earlier?</p> <p>18 MS. CURRY: Object to the form.</p> <p>19 BY MS. GARBER:</p> <p>20 Q You can't see cancer evolving in ovarian</p> <p>21 cancer, can you?</p> <p>22 MS. CURRY: Object to the form.</p> <p>23 THE WITNESS: I don't actually think</p> <p>24 that's true. I think there's some new and emerging</p> <p>25 literature that in particular, for high-grade serous</p>	<p style="text-align: right;">Page 264</p> <p>1 page three, quote, "As we really don't know what</p> <p>2 ovarian cancer looks like as it's developing, unlike</p> <p>3 cancers of the colon, breast, and cervix."</p> <p>4 Isn't that what you said on February</p> <p>5 25th, 2019?</p> <p>6 A Yeah, I think it's an evolving process,</p> <p>7 because I think the different histologic subtypes</p> <p>8 are starting to provide us with clues, but we don't</p> <p>9 really know what it looks like. This is --</p> <p>10 Q So when you look at an ovarian tumor when</p> <p>11 you remove it from a woman, it in no way indicates</p> <p>12 what was happening years earlier during cancer</p> <p>13 transformation, does it?</p> <p>14 MS. CURRY: Object to the form.</p> <p>15 THE WITNESS: I don't --</p> <p>16 MS. GARBER:</p> <p>17 Q Because you can't see that. You can't</p> <p>18 see the transformation of those cells years earlier,</p> <p>19 can you?</p> <p>20 MS. CURRY: Object to the form.</p> <p>21 THE WITNESS: I could still see hallmarks</p> <p>22 of foreign bodies if they were actually there. We</p> <p>23 see in pathology in women that have had surgery</p> <p>24 years before evidence of suture granulomas for</p> <p>25 somebody that might have had surgery before.</p>
<p style="text-align: right;">Page 263</p> <p>1 carcinomas, is giving us a glimpse into the</p> <p>2 evolution from a pre-neoplastic process to ovarian</p> <p>3 cancer.</p> <p>4 That's in particular with what we've been</p> <p>5 able to glean from a lot of the BRCA one and two</p> <p>6 patients who have prophylactic surgery and we've</p> <p>7 been able to identify precursor lesions in those</p> <p>8 patients.</p> <p>9 So I think that might have been true five</p> <p>10 years ago. I don't think that's necessarily true</p> <p>11 now.</p> <p>12 BY MS. GARBER:</p> <p>13 Q Was it true on February 25th, 2019?</p> <p>14 MS. CURRY: Object to the form.</p> <p>15 THE WITNESS: That we didn't know what it</p> <p>16 looks like? I think we don't know what it looks</p> <p>17 like for all cases of ovarian cancer. I think with</p> <p>18 respect to high-grade serous carcinomas, we're</p> <p>19 starting to learn.</p> <p>20 BY MS. GARBER:</p> <p>21 Q If you could turn to page three of your</p> <p>22 expert report, Doctor.</p> <p>23 A Sure.</p> <p>24 Q As to what cancer looks like as it's</p> <p>25 developing, don't you indicate at the bottom of</p>	<p style="text-align: right;">Page 265</p> <p>1 Somebody that might have had a unilateral</p> <p>2 salpingo-oophorectomy and had staples in order to</p> <p>3 operate on her, we see evidence of that even years</p> <p>4 later when they have cancer. So those markers of</p> <p>5 inflammation and responses to foreign bodies don't</p> <p>6 go away just because the patient has cancer.</p> <p>7 BY MS. GARBER:</p> <p>8 Q You can't look at a cancerous tumor and</p> <p>9 say what induced that cancer by looking at it today,</p> <p>10 cellularly, can you?</p> <p>11 MS. CURRY: Object to the form.</p> <p>12 THE WITNESS: I agree with that. I</p> <p>13 don't -- I don't know what induced that particular</p> <p>14 cancer. I agree with that.</p> <p>15 MS. GARBER: Thank you.</p> <p>16 THE WITNESS: Can we take a break?</p> <p>17 MS. GARBER: Sure.</p> <p>18 THE VIDEOGRAPHER: The time is now 3:48.</p> <p>19 Going off the record.</p> <p>20 (Break in the deposition taken at 3:49 p.m.)</p> <p>21 0o0</p> <p>22 (The deposition resumed at 4:10 p.m.)</p> <p>23 0o0</p> <p>24 THE VIDEOGRAPHER: Time is now 4:09.</p> <p>25 Back on the record.</p>

<p style="text-align: right;">Page 266</p> <p>1 BY MS. GARBER:</p> <p>2 Q Doctor, at page 20 of your report, in the</p> <p>3 first full paragraph near the top, you indicate that</p> <p>4 "If talc induces ovarian cancer by causing chronic</p> <p>5 inflammation, then studies examining the use of</p> <p>6 anti-inflammatory agents such as NSAIDS and aspirin</p> <p>7 should show a decreased risk of developing ovarian</p> <p>8 cancer with regular use of these agents."</p> <p>9 Did I read that correctly?</p> <p>10 A Yes.</p> <p>11 Q Did you cite in your expert report</p> <p>12 references to any data looking at NSAIDS and aspirin</p> <p>13 by way of risk of ovarian cancer?</p> <p>14 A Yes.</p> <p>15 Q Okay. And which studies did you cite?</p> <p>16 Are those 13, 15, and 91?</p> <p>17 A Yes, along with reference two.</p> <p>18 Q Doctor, in your references, I could not</p> <p>19 find where you had cited a 2018 paper by the author</p> <p>20 Qiao, Q-I-A-O; is that correct? You did not cite</p> <p>21 that paper?</p> <p>22 A I did not.</p> <p>23 Q Did you perform a comprehensive review of</p> <p>24 the literature looking at NSAIDS and aspirin and the</p> <p>25 potential reduction for risk of ovarian cancer?</p>	<p style="text-align: right;">Page 268</p> <p>1 Q So with regard to the Qiao paper, I</p> <p>2 will -- I don't know how to pronounce it. I'm</p> <p>3 guessing it's Qiao. I'm going to mark that as</p> <p>4 Exhibit 22.</p> <p>5 (C. Saenz Exhibit 22 was marked for</p> <p>6 identification.)</p> <p>7 BY MS. GARBER:</p> <p>8 Q Doctor, I know you haven't read this</p> <p>9 paper. But in the abstract in the conclusions, are</p> <p>10 the conclusions that as cited by these study</p> <p>11 authors, these findings suggest that aspirin use is</p> <p>12 associated with a reduced risk of gastric,</p> <p>13 esophageal, colorectal, pancreatic, ovarian,</p> <p>14 endometrial, breast and prostate cancers and small</p> <p>15 intestine, neuroendocrine tumors?</p> <p>16 A That's the conclusion that the authors</p> <p>17 put there; yes.</p> <p>18 Q So this study, does this look like this</p> <p>19 was a meta-analysis study?</p> <p>20 A That's what it says in the title.</p> <p>21 Q So this was published in 2018, and it is</p> <p>22 a meta-analysis of the association between aspirin</p> <p>23 use and risk of certain cancers when included</p> <p>24 ovarian cancer; correct?</p> <p>25 A Yes, that's one of the things they</p>
<p style="text-align: right;">Page 267</p> <p>1 MS. CURRY: Object to the form.</p> <p>2 THE WITNESS: Yes.</p> <p>3 BY MS. GARBER:</p> <p>4 Q Tell me about that comprehensive review</p> <p>5 of the literature. What did you do?</p> <p>6 A I went to search engines and typed in</p> <p>7 ovarian cancer and NSAIDS.</p> <p>8 Q Did you type in ovarian cancer and</p> <p>9 aspirin?</p> <p>10 A Yes. Aspirin is an NSAID.</p> <p>11 Q But they seem to break it out in the</p> <p>12 literature.</p> <p>13 A Not always.</p> <p>14 Q Okay. Did you do any other search terms</p> <p>15 with regard to ovarian cancer and NSAIDS?</p> <p>16 A Well, I didn't just type NSAIDS because I</p> <p>17 was concerned that if that acronym wasn't in there,</p> <p>18 that it might not come up. So I also typed in</p> <p>19 Tylenol, acetaminophen, ibuprofen, and what else did</p> <p>20 I type in. I think I even looked to see if Celebrex</p> <p>21 was in there, yeah.</p> <p>22 ///</p> <p>23 ///</p> <p>24 ///</p> <p>25 ///</p>	<p style="text-align: right;">Page 269</p> <p>1 examined.</p> <p>2 Q What was the finding by way of reduction</p> <p>3 of risk with regard to ovarian cancer?</p> <p>4 A The authors report that the risk of</p> <p>5 ovarian cancer decreased by 11 percent.</p> <p>6 Q It was statistically significant, wasn't</p> <p>7 it?</p> <p>8 A They reported that that finding was</p> <p>9 statistically significant; correct.</p> <p>10 MS. GARBER: Let's look at another paper.</p> <p>11 This I'll mark as Exhibit 24. And this paper, the</p> <p>12 lead author is Trabert, T-R-A-B-E-R-T, et al.,</p> <p>13 titled "Aspirin, Nonsteroidal, Nonaspirin,</p> <p>14 Nonsteroidal Anti-Inflammatory Drug and</p> <p>15 Acetaminophen Use and the Risk of Invasive</p> <p>16 Epithelial Ovarian Cancer, a Pooled Analysis in the</p> <p>17 Ovarian Cancer Association Consortium."</p> <p>18 BY MS. GARBER:</p> <p>19 Q Did I read that correctly?</p> <p>20 A Yes.</p> <p>21 MS. CURRY: Did we skip Exhibit 23?</p> <p>22 MS. GARBER: Did I miss one?</p> <p>23 THE WITNESS: Yes.</p> <p>24 MS. GARBER: Oh, I did. Let's replace.</p> <p>25 MS. SHARKO: So Trabert is now 23?</p>

Page 270	Page 272
<p>1 MS. GARBER: Trabert 2013 is now Exhibit</p> <p>2 23.</p> <p>3 MS. CURRY: I think this is a 2014 --</p> <p>4 MS. GARBER: You're right. It's at the</p> <p>5 top. All right. So Trabert 2014, part of the</p> <p>6 title, "Aspirin, Nonaspirin, Nonsteroidal</p> <p>7 Anti-Inflammatory Drug," is now Exhibit 23.</p> <p>8 (C. Saenz Exhibit 23 was marked for</p> <p>9 identification.)</p> <p>10 BY MS. GARBER:</p> <p>11 Q Doctor, I don't see that this paper is on</p> <p>12 your reference list either; is that correct?</p> <p>13 A Correct.</p> <p>14 Q And nonsteroidal anti-inflammatory drug</p> <p>15 is the long name for the acronym, NSAIDS; correct?</p> <p>16 A Correct.</p> <p>17 Q So your literature search should have</p> <p>18 turned up this paper because NSAID was in the title;</p> <p>19 correct?</p> <p>20 A It depends. It's not always that simple.</p> <p>21 I understand that's it's there in the title, but if</p> <p>22 you type in NSAIDS, it doesn't always come up.</p> <p>23 Sometimes different permutations of your search will</p> <p>24 yield different results.</p> <p>25 Q In the authors' conclusions, in the</p>	<p>1 the left-hand column, indicates that it included</p> <p>2 more than 7500 ovarian cancer cases from 12</p> <p>3 population based case control studies; correct?</p> <p>4 A I'm sorry, where are we?</p> <p>5 Q On page two.</p> <p>6 A Yeah.</p> <p>7 Q Left-hand column at the top.</p> <p>8 A Oh, left-hand column.</p> <p>9 Q "We concluded."</p> <p>10 A We conducted?</p> <p>11 Q Yeah. It indicates that the study</p> <p>12 included more than 7500 ovarian cancer cases from 12</p> <p>13 population based case control studies; right?</p> <p>14 A Right.</p> <p>15 Q At the last page, nine of 11, it</p> <p>16 indicates, "In summary, this pooled analysis</p> <p>17 supports the hypothesis that regular aspirin use</p> <p>18 reduces ovarian cancer risk. Specifically we report</p> <p>19 a statistically significant decreased risk of</p> <p>20 ovarian cancer with daily use of aspirin. Further</p> <p>21 biological and pharmaceutical" -- sorry,</p> <p>22 pharmacological research is necessary to understand</p> <p>23 the mechanisms of ovarian cancer risk reduction by</p> <p>24 aspirin."</p> <p>25 Did I read that correctly?</p>
Page 271	Page 273
<p>1 manuscript, it indicates "Aspirin use was associated</p> <p>2 with a reduced risk of ovarian cancer especially</p> <p>3 among daily users of low-dose aspirin. These</p> <p>4 findings suggest that same aspirin regimen proven to</p> <p>5 protect against cardiovascular events and several</p> <p>6 cancers could reduce the risk of ovarian cancer, 20</p> <p>7 to 34 percent, depending upon" -- "depending on</p> <p>8 frequency and dose of use."</p> <p>9 Did I read that correctly?</p> <p>10 A That's their conclusion. The result</p> <p>11 section is what actually has that data. The</p> <p>12 conclusion section doesn't comment on the NSAIDS.</p> <p>13 Q And, Doctor, on the first page of this</p> <p>14 paper, in the second paragraph, does it indicate</p> <p>15 multiple lines of evidence suggest that ovarian</p> <p>16 cancer maybe related to chronic inflammation?</p> <p>17 A So again, that's a statement from the</p> <p>18 introduction section and they're referencing to that</p> <p>19 same Ness paper that actually didn't evaluate</p> <p>20 chronic inflammation but just commented on different</p> <p>21 hypotheses as to carcinogenesis of ovarian cancer.</p> <p>22 This paper is actually very similar in findings, I</p> <p>23 think, to the Barnard paper, which I did reference</p> <p>24 to in my report.</p> <p>25 Q This paper, if you look at page two on</p>	<p>1 A You read that statement correctly, but</p> <p>2 that wasn't the only finding in this study, just</p> <p>3 like it wasn't the only finding in the Barnard</p> <p>4 study, which is why in my report, I talked about the</p> <p>5 literature on NSAIDS being inconsistent.</p> <p>6 Sometimes it looks like it reduces the</p> <p>7 risk. Sometimes it looks like there is no effect.</p> <p>8 Sometimes it looks like there actually was an</p> <p>9 increased risk of developing ovarian cancer. So the</p> <p>10 literature on NSAID use in development of ovarian</p> <p>11 cancer is inconsistent.</p> <p>12 Q How many studies did you review that</p> <p>13 indicated that NSAIDS increased the risk of ovarian</p> <p>14 cancer?</p> <p>15 A Two.</p> <p>16 Q How many studies did you review that</p> <p>17 indicated NSAIDS, including aspirin, reduced the</p> <p>18 risk of ovarian cancer?</p> <p>19 A So the issue is a little bit more complex</p> <p>20 than that because some of the studies don't</p> <p>21 necessarily break out which ones they were talking</p> <p>22 about. I believe the Barnard study looked at</p> <p>23 low-dose aspirin use, daily aspirin use, and then</p> <p>24 NSAIDS, and the results for each of those agents was</p> <p>25 different.</p>

Page 274

1 So in total, I reference, I believe -- is
2 it three or four studies -- four studies in my
3 review that looked at the use of NSAIDS and the
4 development of ovarian cancer. And the literature
5 was inconsistent.
6 Q Do you rely on the studies that show that
7 NSAIDS and aspirin do not reduce the risk to support
8 your opinions that talc does not induce chronic
9 inflammation that leads to ovarian cancer?
10 A No, I rely on the fact that the
11 literature is inconsistent to formulate my opinion
12 that chronic inflammation is the mechanism by which
13 talc would increase the risk of developing ovarian
14 cancer is not true.
15 Q You do admit, though, that is there is
16 peer reviewed, published literature that NSAIDS,
17 including aspirin, have been shown to reduce the
18 risk of ovarian cancer, because they're
19 anti-inflammatories; right?
20 MS. CURRY: Object to the form.
21 BY MS. GARBBER:
22 Q It's the mechanism?
23 A Well, but just within this paper that you
24 just produced as evidence, there's also within the
25 exact same paper showing evidence that NSAIDS don't

Page 275

1 review -- sorry, don't reduce the risk of ovarian
2 cancer.
3 So what's what I mean by inconsistent, is
4 that some components of a study, depending on the
5 agent, show a reduction in risk. Others don't show
6 a reduction in risk, even within the same study, and
7 other studies have shown an increase in risk.
8 So that's actually what I mean by
9 inconsistent.
10 BY MS. GARBBER:
11 Q But you nevertheless conclude based on
12 the data with regard to NSAIDS and aspirin and risk
13 of ovarian cancer, that there is not a mechanism of
14 carcinogenicity by chronic inflammation, don't you?
15 MS. CURRY: Object to the form.
16 THE WITNESS: What I conclude is that the
17 literature on NSAIDS and ovarian cancer does not
18 support the hypothesis of chronic inflammation as
19 the mechanism.
20 If all the literature on NSAIDS
21 consistently showed a reduction in risk across the
22 board in the development of ovarian cancer with
23 regular NSAID use, then I think that would actually
24 go to potentially the biologic plausibility of
25 chronic inflammation as a mechanism. But it does

Page 276

1 not.
2 The fact that the NSAID literature
3 doesn't consistently show a reduction in risk speaks
4 to it likely being some other reason that the
5 literature is showing that, that it's not simply the
6 prevention of chronic inflammation.
7 BY MS. GARBBER:
8 Q Could it be the design of the study?
9 MS. CURRY: Object to the form.
10 THE WITNESS: I think any time we're
11 talking about case control studies, which is what
12 this study, this meta-analysis looks like, this one
13 that you just handed me, Exhibit 23, is a
14 compilation of -- what did we say, 12
15 population-based case control studies. I think
16 there's always the possibility that you've got a
17 confound in that study. That is the reason that you
18 have the findings that you have.
19 But the Barnard study was actually a
20 cohort study. It was prospective. So I don't
21 necessarily think that you're subject to the same
22 compound and recall biases that you might be in a
23 case control study such as Exhibit 23.
24 BY MS. GARBBER:
25 Q So you put more weight on the Barnard

Page 277

1 cohort study than you did the meta-analyses of the
2 data; is that fair, with regard to NSAIDS?
3 A Well, with respect to the studies you
4 just showed me?
5 Q Okay.
6 A I've not had a chance to read these two
7 studies through, so I can't really give you an
8 analysis on that. If we're talking about in a
9 general principle, I do think that a cohort study is
10 more scientifically credible than a case controlled
11 study.
12 Q You've rendered an opinion about what the
13 literature shows by way of consistency with regard
14 to NSAIDS and aspirin without reviewing all of the
15 literature, do you agree?
16 MS. CURRY: Object to the form.
17 THE WITNESS: I believe that I've
18 reviewed a sufficient amount of the literature to
19 render the opinion that I've rendered which is that
20 the literature is inconsistent and, in fact, the two
21 references that you just showed me are consistent
22 with my opinion that the literature on NSAIDS is
23 inconsistent.
24 BY MS. GARBBER:
25 Q Doctor, do you think it's possible to

<p style="text-align: right;">Page 278</p> <p>1 render an accurate opinion without reviewing the</p> <p>2 totality of the literature on a given topic?</p> <p>3 MS. CURRY: Object to the form.</p> <p>4 THE WITNESS: I think that you can review</p> <p>5 a sufficient amount of literature to render an</p> <p>6 opinion as long as the literature that you're</p> <p>7 reviewing encompasses the breath and depth of the</p> <p>8 science that is out there.</p> <p>9 BY MS. GARBER:</p> <p>10 Q Do you remember in the Echeverria report</p> <p>11 what your opinions were with regard to the risk of</p> <p>12 obesity and serous ovarian cancer?</p> <p>13 A So I'm not entirely sure what I said in</p> <p>14 that report. I'd be happy to look at it. I'm not</p> <p>15 entirely sure I commented specifically on serous</p> <p>16 ovarian cancer in the Echeverria report.</p> <p>17 Q In this report, do you have an opinion as</p> <p>18 to the risk of obesity as it pertains to serous</p> <p>19 ovarian cancer?</p> <p>20 A So I think the literature on obesity</p> <p>21 actually does -- well, I think it's inconsistent. I</p> <p>22 think that it's somewhat weak. I think that the</p> <p>23 strength of the association is still in the range of</p> <p>24 roughly 1.2 to 1.3. And I believe the histologic</p> <p>25 subtypes that are most often associated with obesity</p>	<p style="text-align: right;">Page 280</p> <p>1 BY MS. GARBER:</p> <p>2 Q Let's put a number two on the second</p> <p>3 page.</p> <p>4 A Okay.</p> <p>5 Q Then let's put a page three. And</p> <p>6 page four.</p> <p>7 A Okay.</p> <p>8 Q That's all I'm going to mark as from the</p> <p>9 report of Cheryl Saenz, MD, with regard to the</p> <p>10 Echeverria report. We will just mark the first four</p> <p>11 pages; okay?</p> <p>12 A Ma'am, there's patient identifier</p> <p>13 information on page two.</p> <p>14 Q Okay. We will then just mark page four</p> <p>15 of the Echeverria report.</p> <p>16 A Okay. I just --</p> <p>17 Q Thank you for saying that. Okay.</p> <p>18 With regard to your obesity opinion, in</p> <p>19 this expert report, do you indicate that the data</p> <p>20 shows an increased risk for high-grade serous?</p> <p>21 A In this report?</p> <p>22 Q In the Echeverria report, which we've</p> <p>23 marked as Exhibit 24.</p> <p>24 A No. I don't comment on it increasing the</p> <p>25 development of high-grade serous. I comment on it</p>
<p style="text-align: right;">Page 279</p> <p>1 do not include serous.</p> <p>2 MS. GARBER: I'm going to mark as</p> <p>3 Exhibit 24 your expert report from the Echeverria</p> <p>4 matter.</p> <p>5 (C. Saenz Exhibit 24 was marked for</p> <p>6 identification.)</p> <p>7 BY MS. GARBER:</p> <p>8 Q If you could turn to -- you didn't number</p> <p>9 your pages, but it's about fourth page in.</p> <p>10 MS. SHARKO: Is that protected</p> <p>11 information in it?</p> <p>12 MS. GARBER: Not in this section -- you</p> <p>13 know, that's a good point. Thank you very much,</p> <p>14 Ms. Sharko. You know what we'll do is, I will</p> <p>15 take --</p> <p>16 MS. SHARKO: Maybe give the witness the</p> <p>17 whole report, question her, and then only mark pages</p> <p>18 of it.</p> <p>19 MS. GARBER: Thank you. Well, I don't</p> <p>20 have pages. You know what, let's do, Dr. Saenz,</p> <p>21 let's put just a number, just if you could do this,</p> <p>22 put a number one on the first page at the bottom.</p> <p>23 THE WITNESS: On the first page? I'm</p> <p>24 sorry. Okay.</p> <p>25 ///</p>	<p style="text-align: right;">Page 281</p> <p>1 portending a worse prognosis in terms of mortality</p> <p>2 for high-grade serous.</p> <p>3 Q Was it your opinion that obesity</p> <p>4 increases high-grade serous in that case?</p> <p>5 A In terms of that incidence or the</p> <p>6 mortality from?</p> <p>7 Q The incidence.</p> <p>8 A Not the incidence. The mortality from.</p> <p>9 Q Is it your opinion in the MDL report that</p> <p>10 obesity increases the risk for high-grade serous, or</p> <p>11 serous ovarian cancer?</p> <p>12 A The incidence?</p> <p>13 Q Yes.</p> <p>14 A No.</p> <p>15 Q Is it your opinion that obesity increases</p> <p>16 the mortality for high-grade serous?</p> <p>17 A It's my opinion that obesity increases</p> <p>18 the mortality for basically all of the ovarian</p> <p>19 cancers.</p> <p>20 Q Do you say that in your expert report?</p> <p>21 A I do.</p> <p>22 Q Okay.</p> <p>23 A Ma'am, may I ask, what should I do with</p> <p>24 this then?</p> <p>25 Q Thank you. Moving on. Okay. Let's talk</p>

<p style="text-align: right;">Page 282</p> <p>1 about a different topic for awhile.</p> <p>2 Is it your opinion that the data do not</p> <p>3 support a dose response with regard to talcum</p> <p>4 powder, genital talcum powder exposure and risk of</p> <p>5 ovarian cancer?</p> <p>6 A Yes, that's correct.</p> <p>7 Q You reviewed the Berge study in</p> <p>8 connection with your expert report; correct?</p> <p>9 A The meta-analysis?</p> <p>10 Q Yes.</p> <p>11 A Yes.</p> <p>12 MS. GARBBER: I will mark the Berge paper</p> <p>13 as Exhibit 25.</p> <p>14 (C. Saenz Exhibit 25 was marked for</p> <p>15 identification.)</p> <p>16 BY MS. GARBBER:</p> <p>17 Q Doctor, the title of this paper is</p> <p>18 "Genital Use of Talc and Risk of Ovarian Cancer, a</p> <p>19 Meta-Analysis"; correct?</p> <p>20 A Correct.</p> <p>21 Q If you turn to page -- let's just look at</p> <p>22 the first page. In the abstract, the study authors</p> <p>23 indicate, "This meta-analysis resulted" --</p> <p>24 A I'm sorry, ma'am. On the first page,</p> <p>25 where are we? In the second column?</p>	<p style="text-align: right;">Page 284</p> <p>1 meta-analysis resulted in a weak but statistically</p> <p>2 significant association between genital talc use in</p> <p>3 ovarian cancer, which appears to be limited to</p> <p>4 serous carcinoma with suggestion of a dose</p> <p>5 response."</p> <p>6 If it says that, do you disagree with the</p> <p>7 study authors?</p> <p>8 MS. CURRY: Do you have a copy of that</p> <p>9 version?</p> <p>10 MS. GARBBER: No, I just said that I</p> <p>11 don't.</p> <p>12 MS. CURRY: You don't have it.</p> <p>13 MS. GARBBER: She had it on her reference</p> <p>14 list, and I don't. I put it in hypothetical.</p> <p>15 BY MS. GARBBER:</p> <p>16 Q If the study authors say that, do you</p> <p>17 disagree with that?</p> <p>18 A So I have to look at the paper to see</p> <p>19 exactly what we're looking at and to see where</p> <p>20 they're saying the suggestion. Because the paper</p> <p>21 you've just put in front of me, by the same group,</p> <p>22 with the same title, actually says that the</p> <p>23 heterogeneity of results by study design and the</p> <p>24 lack of a trend for duration and frequency of use</p> <p>25 detract from a causal interpretation of the</p>
<p style="text-align: right;">Page 283</p> <p>1 Q At the top, in the abstract.</p> <p>2 A Okay.</p> <p>3 Q Right-hand column, it indicates, "This</p> <p>4 meta-analysis." Do you see that?</p> <p>5 A Yes, thank you.</p> <p>6 Q "This meta-analysis resulted in weak but</p> <p>7 statistically significant association between</p> <p>8 genital use of talc in ovarian cancer, which appears</p> <p>9 to be a limited to serous" -- sorry.</p> <p>10 A No worries.</p> <p>11 Q I gave you the wrong version.</p> <p>12 A Give you this back?</p> <p>13 Q No. Let's just hang on.</p> <p>14 Your references indicate the Berge paper</p> <p>15 that was published in the European Journal of Cancer</p> <p>16 Prevention in 2018; correct? It's at page 32.</p> <p>17 A Yes.</p> <p>18 Q The citation there is Volume 27(3),</p> <p>19 May 2018, pages 248 to 257; correct?</p> <p>20 A Correct.</p> <p>21 Q So you have read that publication of the</p> <p>22 Berge study; correct?</p> <p>23 A Correct.</p> <p>24 Q So, Doctor, I will represent to you that</p> <p>25 at the bottom of the abstract, the study says, "This</p>	<p style="text-align: right;">Page 285</p> <p>1 association.</p> <p>2 MS. GARBBER: Would you object if I give</p> <p>3 her a highlighted version that she can look at for</p> <p>4 purposes of this question?</p> <p>5 MS. CURRY: No objection.</p> <p>6 MS. GARBBER: I can make a clean copy of</p> <p>7 it so that doesn't show up.</p> <p>8 MS. CURRY: Okay.</p> <p>9 BY MS. GARBBER:</p> <p>10 Q Doctor, do you see in the abstract where</p> <p>11 I read from, at the bottom, where it says "This</p> <p>12 meta-analysis"?</p> <p>13 A "This meta-analysis resulted in a weak</p> <p>14 but statistically significant association between</p> <p>15 genital use of talc and ovarian cancer, which</p> <p>16 appears to be limited to serous carcinoma with</p> <p>17 suggestion of a dose response."</p> <p>18 Q Do you disagree with the study authors,</p> <p>19 the study provided a suggestion of a dose response?</p> <p>20 MS. CURRY: Object to the form.</p> <p>21 THE WITNESS: So I don't disagree with</p> <p>22 the suggestion. I don't think that demonstrates a</p> <p>23 dose response, because the authors also go on to</p> <p>24 say, "The heterogeneity of results by study design,</p> <p>25 however, detracts from a causal interpretation of</p>

<p style="text-align: right;">Page 286</p> <p>1 this association."</p> <p>2 MS. GARBER: Motion to strike as</p> <p>3 nonresponsive.</p> <p>4 BY MS. GARBER:</p> <p>5 Q Doctor, if you could now turn to about</p> <p>6 halfway through the paper.</p> <p>7 A Which paper, ma'am, the one that I just</p> <p>8 got handed or the one before?</p> <p>9 Q The one that you just got handed --</p> <p>10 A Okay.</p> <p>11 Q -- which we will mark as Exhibit -- we</p> <p>12 will change and we will make that Exhibit 25.</p> <p>13 MS. CURRY: I think there's been</p> <p>14 testimony on Exhibit 25. Do you want to change --</p> <p>15 do you want to mark this 26?</p> <p>16 MS. GARBER: Let's make that -- let's</p> <p>17 just make that, yeah, 26.</p> <p>18 (C. Saenz Exhibit 26 was marked for</p> <p>19 identification.)</p> <p>20 BY MS. GARBER:</p> <p>21 Q So Doctor, Exhibit 26 is now the Berge</p> <p>22 paper which is published in the European journal of</p> <p>23 Cancer Prevention, Volume 273, May 2018; correct?</p> <p>24 A Yes, ma'am.</p> <p>25 Q That's the same one that's listed on your</p>	<p style="text-align: right;">Page 288</p> <p>1 THE WITNESS: I don't necessarily know</p> <p>2 that, because I don't know what it's being compared</p> <p>3 against. If it's being compared against never use</p> <p>4 versus another time period, my answer would be</p> <p>5 different.</p> <p>6 BY MS. GARBER:</p> <p>7 Q Okay. Can you go back to the Schildkraut</p> <p>8 paper that we marked as Exhibit 7, please. If you</p> <p>9 turn --</p> <p>10 A Give me a second, ma'am.</p> <p>11 Q Sure.</p> <p>12 A Okay.</p> <p>13 Q If you turn to page 1416 of that</p> <p>14 publication --</p> <p>15 A Yes, ma'am.</p> <p>16 Q -- on the left-hand column, about just a</p> <p>17 little below halfway down, it begins with "The</p> <p>18 results." Do you see where I am?</p> <p>19 A No.</p> <p>20 Q It's about three-quarters of the way down</p> <p>21 the results.</p> <p>22 A Oh.</p> <p>23 Q See that?</p> <p>24 A Oh, sorry, yes. The beginning of the</p> <p>25 paragraph -- yes.</p>
<p style="text-align: right;">Page 287</p> <p>1 reference list in your expert report?</p> <p>2 A Yes, ma'am.</p> <p>3 Q All right. Now, if I could have you turn</p> <p>4 to table three of that study.</p> <p>5 A I don't see a table three. Am I missing</p> <p>6 something?</p> <p>7 Q Go back one page.</p> <p>8 A Sorry; yes.</p> <p>9 Q That table three is titled "Duration and</p> <p>10 Frequency of Use of Genital Talc, Results of the</p> <p>11 Meta-Analysis." Do you see that?</p> <p>12 A No. Oh, sorry, "Duration and Frequency</p> <p>13 of Use of Genital Talc Results in Meta-Analysis."</p> <p>14 Yes.</p> <p>15 Q For the duration of ten years, the</p> <p>16 relative risk was 1.16 and statistically</p> <p>17 significant; correct?</p> <p>18 A Yes.</p> <p>19 Q And the frequency of use defined as one</p> <p>20 time per week, showed a relative risk of 1.05, also</p> <p>21 statistically significant; correct?</p> <p>22 A Yes.</p> <p>23 Q So these data support a suggestion of</p> <p>24 dose response, don't they?</p> <p>25 MS. CURRY: Object to the form.</p>	<p style="text-align: right;">Page 289</p> <p>1 Q Yes. The study authors indicate here,</p> <p>2 "The results of the current study show that genital</p> <p>3 powder use was associated with ovarian cancer risk</p> <p>4 in African-American women and are consistent with</p> <p>5 localized chronic inflammation in the ovary due to</p> <p>6 particulates that travel through a direct</p> <p>7 transvaginal route." Did I read that correctly?</p> <p>8 A You read that component of the discussion</p> <p>9 section; yes.</p> <p>10 Q The authors also say, "The dose response</p> <p>11 observed for duration of genital powder use provides</p> <p>12 further evidence for the relationship between</p> <p>13 genital powder and overall epithelial ovarian cancer</p> <p>14 risk."</p> <p>15 Did I read that correctly?</p> <p>16 A That is what the author said, but what</p> <p>17 their data actually shows, their analysis for their</p> <p>18 dose response curve was not done correctly. And so</p> <p>19 I don't agree that this paper actually shows a dose</p> <p>20 response.</p> <p>21 Q Here again, you agree -- you disagree</p> <p>22 with study authors who actually conducted the study?</p> <p>23 A I do, ma'am, because this study looked at</p> <p>24 applications without pulling out the never-users.</p> <p>25 So the weight of having a statistically significant</p>

<p style="text-align: right;">Page 290</p> <p>1 finding with more use is influenced by the never-use 2 population remaining in the analysis. 3 Q Let's look at Cramer 2016. That was 4 another study you cited in your reference list; 5 correct? 6 A Yes, ma'am. 7 (C. Saenz Exhibit 27 was marked for 8 identification.) 9 BY MS. GARBER: 10 Q Dr. Cramer was one of the -- 11 A This is 27. 12 Q Thank you. Exhibit 27 is the Cramer 2016 13 paper titled "The Association Between Talc Use in 14 Ovarian Cancer Retrospective Case Control Study in 15 Two US States"; right? 16 A Yes. 17 Q Dr. Cramer was the first study author in 18 1982 to find a statistically significant associated 19 risk between genital talc use and ovarian cancer; 20 right? 21 A I believe that he's the first person to 22 publish that, yes, ma'am. 23 Q He has since published a number of 24 studies about the issues surrounding talc and 25 ovarian cancer, including this study in 2016;</p>	<p style="text-align: right;">Page 292</p> <p>1 THE WITNESS: The Terry pooled analysis, 2 I think, from a standpoint of the way that that 3 study was conducted, I think it was scientifically 4 sound. 5 BY MS. GARBER: 6 Q Any others? There's about 30 of them; 7 right? 8 MS. CURRY: Object to the form. 9 THE WITNESS: The case control studies, I 10 don't have criticisms of all of them. It's just 11 when I'm reviewing them, I review the data in its 12 entirety, particularly looking for consistencies 13 within the study, if it's reporting on things that 14 are claimed in the conclusions. 15 BY MS. GARBER: 16 Q Do you have any criticisms of any of the 17 data that didn't find a statistically significant 18 increased risk between genital talc and epithelial 19 ovarian cancer? 20 MS. CURRY: Object to the form. 21 THE WITNESS: I'm sure I -- 22 MS. GARBER: Or are your criticisms just 23 limited to the positive data? 24 MS. CURRY: Object to the form. 25 THE WITNESS: No, my criticisms are not</p>
<p style="text-align: right;">Page 291</p> <p>1 correct? 2 MS. CURRY: Object to the form. 3 THE WITNESS: He -- he has published a 4 number of studies, yes. And -- yes, this study was 5 publish in yeah, 2016. 6 BY MS. GARBER: 7 Q Do you have any reason to doubt the 8 reliability of this particular study? 9 MS. CURRY: Object to the form. 10 THE WITNESS: I think there are problems 11 with this study, particularly with respect to the 12 reporting of a dose-response curve as we were just 13 discussing. 14 BY MS. GARBER: 15 Q Can you name any positive study that 16 supports an association between genital talc use and 17 ovarian cancer that you don't think has a problem? 18 A So I actually think the Terry pooled 19 analysis -- 20 Q Is that in your eyes? 21 A Yeah. I can just sit back a little. 22 MS. CURRY: Are you okay on the video? 23 THE VIDEOGRAPHER: Yeah, they're all 24 down. Tried to pull them down more. They're not 25 blocking.</p>	<p style="text-align: right;">Page 293</p> <p>1 just limited to the positive data. 2 BY MS. GARBER: 3 Q Let's look at the Terry 2016 study. 4 MS. CURRY: Do you mean Cramer? 5 THE WITNESS: We're looking at Terry 2013 6 or Cramer 2016? 7 MS. GARBER: Let's look at the Cramer 8 2016 study. 9 THE WITNESS: Okay. 10 MS. SHARKO: Are you okay with the sun? 11 THE WITNESS: I'm okay. If I need to -- 12 I can back up. Right now, I'm okay. 13 THE VIDEOGRAPHER: Doctor, try to move a 14 little way this way. That's fine. 15 THE WITNESS: Move this way? Yeah, 16 that's -- I'm going to sit back here. 17 THE VIDEOGRAPHER: That's better 18 actually. 19 THE WITNESS: You got the right side? 20 MS. GARBER: That's all off the record. 21 THE REPORTER: Unfortunately, it is on. 22 BY MS. GARBER: 23 Q Doctor, if you can turn to page 337 of 24 this study. 25 A Yes, ma'am.</p>

<p style="text-align: right;">Page 294</p> <p>1 Q Start with page 335 to get the full 2 sentence. The very last sentence on 335 indicates, 3 "An odds ratio of 1.49 with a confidence interval of 4 1.06 to 2.10 was associated with more than 20 talc 5 years (greater than 7200 applications) and a dose 6 response." 7 A That's what they wrote. 8 Q Do you disagree with the study authors in 9 this case that the results supported a dose 10 response? 11 A So I don't disagree with the finding, 12 that that's the odds ratio. But I do disagree with 13 the statement that this analysis, which is in the 14 top part of the table one, looking at total genital 15 applications among only those who reported months 16 per year per use, that analysis, that grouping, does 17 not support a dose response with each of those 18 intervals of applications. 19 The only -- there are two, actually, that 20 report statistical significance. The one of the 361 21 to 1800 applications, and the greater than 7200 that 22 you just reported. But the interval in between 23 those two does not achieve statistical significance 24 and, in fact, has an odds ratio even lower than less 25 application.</p>	<p style="text-align: right;">Page 296</p> <p>1 MS. CURRY: Object to the form. 2 THE WITNESS: Not with respect to talc 3 and not with respect to having a lesser exposure 4 cause a cancer as we're looking at in this 5 circumstance, an intermediate exposure not causing 6 cancer and then the higher exposure causing the 7 cancer. It -- I'm not aware of anything that would 8 say an intermediate exposure of a carcinogenic agent 9 is safe when a lower exposure is not. 10 BY MS. GARBER: 11 Q You're not a toxicologist, though; right? 12 A No, ma'am. 13 Q If you turn to page 345, there is a 14 summary, that says, "In summary, the study on talc 15 in epithelial ovarian" -- 16 A I'm sorry, can you slow down and let me 17 get there. 18 Q Sure. 19 A Thank you. 20 Q 345, left-hand column. It reads, "In 21 summary, this study on talc and epithelial ovarian 22 cancer has contributed to the following perspectives 23 with some new regarding this association." 24 And the first one reads, "Overall, there 25 is an association between genital talc use an EOC</p>
<p style="text-align: right;">Page 295</p> <p>1 So I don't believe that this grouping, 2 the analysis of the total applications actually 3 supports a dose response. 4 Q You make that assumption, because you 5 assume that the dose response needs to be linear, 6 don't you? 7 MS. CURRY: Object to the form. 8 THE WITNESS: No, that's actually not 9 true. I'm drawing that opinion from the fact that a 10 lower number of applications was reported as a 11 statistically significant finding, and then the 12 intermediate number of applications actually wasn't 13 statistically significant and had a lower odds 14 ratio. And then the higher number of applications 15 had statistical significance. 16 So it's not a matter of threshold 17 response per se. It's a matter of the fact that the 18 statistically significant findings are interrupted 19 by nonstatistically significant findings of an 20 actually lower odds ratio. 21 BY MS. GARBER: 22 Q Are you aware of any toxicology 23 principles that would support that you don't have to 24 have a linear increase. It can be in the shape of 25 go up, go down, then go back up?</p>	<p style="text-align: right;">Page 297</p> <p>1 and a significant trend with increasing talc years 2 of use." 3 Did you disagree with that? 4 A I don't believe this paper supports that 5 contention. 6 Q So yet again here, you're disagreeing 7 with a study author that has actually conducted a 8 study with regard to genital talc use in ovarian 9 cancer? 10 MS. CURRY: Object to the form. 11 THE WITNESS: I disagree with the 12 statement in the conclusion section, because the 13 table that is presented actually as the data does 14 not support that statement. 15 MS. GARBER: Let's mark the Terry paper 16 as 28. 17 (C. Saenz Exhibit 28 was marked for 18 identification.) 19 BY MS. GARBER: 20 Q Doctor, you looked at this study; 21 correct? 22 A I read this study, yes. 23 Q The title is "Genital Powder Use in the 24 Risk of Ovarian Cancer, a Pooled Analysis, of 25 8525 Cases and 9859 Controls."</p>

<p style="text-align: right;">Page 298</p> <p>1 A Correct.</p> <p>2 Q With regard to dose response at page six,</p> <p>3 the authors address -- I'm sorry, under discussion.</p> <p>4 Under discussion that begins "The biologic</p> <p>5 plausibility."</p> <p>6 Do you see where I am?</p> <p>7 A Yes.</p> <p>8 Q The authors here address some of the</p> <p>9 issues that I was just raising with regard to it may</p> <p>10 not be a linear dose response, don't they?</p> <p>11 MS. CURRY: Object to the form.</p> <p>12 THE WITNESS: You would need to point out</p> <p>13 for me exactly what you're referring to.</p> <p>14 MS. GARBER: Okay.</p> <p>15 BY MS. GARBER:</p> <p>16 Q The Terry authors indicate "The biologic</p> <p>17 plausibility for the observed association between</p> <p>18 genital talc use and ovarian cancer risk has been</p> <p>19 challenged because evidence for a dose response has</p> <p>20 been inconsistent."</p> <p>21 Gives some citation. It says "The lack</p> <p>22 of significant dose response may reflect the</p> <p>23 difficulty inherent in accurate recollection of</p> <p>24 specific details of frequency and duration of</p> <p>25 genital powder use."</p>	<p style="text-align: right;">Page 300</p> <p>1 is carcinogenic. But the literature on talc and</p> <p>2 developing ovarian cancer, that's not my criticisms</p> <p>3 of the studies that lack a dose response curve.</p> <p>4 My criticisms of the studies that lack a</p> <p>5 dose response curve are either one, they fail to</p> <p>6 pool the never-users out of the analysis, so the</p> <p>7 weight of seeing a dose response is actually</p> <p>8 influenced by the fact that the never-users still</p> <p>9 remain in the analysis.</p> <p>10 And two, there are studies such as Cramer</p> <p>11 2016 that we just talked about, that a lower dose</p> <p>12 seems to have an association between ovarian cancer,</p> <p>13 but an intermediate dose does not. And then a</p> <p>14 higher dose does have that statistical significant</p> <p>15 finding so I believe what Terry is saying, is that</p> <p>16 may be not linear. It may be threshold. But that</p> <p>17 doesn't alter the findings in Cramer. It doesn't</p> <p>18 alter the way that Schildkraut did the analysis.</p> <p>19 So those are my criticisms. I don't</p> <p>20 think it's entirely explained by what Terry is</p> <p>21 offering here in the discussion section.</p> <p>22 BY MS. GARBER:</p> <p>23 Q Do you agree that the literature -- there</p> <p>24 are literature that support a dose response?</p> <p>25 A I do not believe that there's any</p>
<p style="text-align: right;">Page 299</p> <p>1 They go on to say "Also, because not all</p> <p>2 powder products contain talc, various products may</p> <p>3 differ in their potential cardiogenic effects."</p> <p>4 MS. CURRY: Carcinogenic effects.</p> <p>5 MS. GARBER: "Carcinogenic effects.</p> <p>6 Alternatively, the association between genital</p> <p>7 powder exposure and ovarian cancer risk may not be</p> <p>8 linear, and modest exposure maybe sufficient to</p> <p>9 increase cancer risk."</p> <p>10 BY MS. GARBER:</p> <p>11 Q Did I read that correctly with counsel's</p> <p>12 help?</p> <p>13 A That, and earlier I think you missed a</p> <p>14 word. It wasn't genital talc use. It was genital</p> <p>15 powder use in the first sentence, but otherwise;</p> <p>16 yes.</p> <p>17 Q Okay. Do you agree with the authors that</p> <p>18 the dose response results that are seen in the</p> <p>19 literature and the inconsistency of those may</p> <p>20 reflect that there's not a linear response, but yet</p> <p>21 there can still be carcinogenicity?</p> <p>22 MS. CURRY: Object to the form.</p> <p>23 THE WITNESS: So I believe that the lack</p> <p>24 of a linear response may be true, and it may be that</p> <p>25 a threshold dose is the mechanism by which something</p>	<p style="text-align: right;">Page 301</p> <p>1 literature that actually has shown a dose response</p> <p>2 where the dose response calculations have been done</p> <p>3 correctly.</p> <p>4 Q You believe the failure to pull the</p> <p>5 never-users out of the equation operates to increase</p> <p>6 the odds ratio?</p> <p>7 MS. CURRY: Object to the form.</p> <p>8 THE WITNESS: I believe that the failure</p> <p>9 to pull the never-users out of the calculation of a</p> <p>10 dose response analysis does influence that analysis</p> <p>11 towards showing a higher odds ratio for increased</p> <p>12 applications or longer duration or increased</p> <p>13 frequency.</p> <p>14 BY MS. GARBER:</p> <p>15 Q Why is that if they've never used talc?</p> <p>16 A Because the dose, if you're looking at</p> <p>17 just two applications, let's say that you're looking</p> <p>18 at less than 5,000 applications or more than 5,000</p> <p>19 applications, the lower odds ratio that's calculated</p> <p>20 with less than 5,000 applications is influenced by</p> <p>21 the never-users still being in there.</p> <p>22 The higher odds ratio that you see when</p> <p>23 you calculate the odds ratio for more than 5,000</p> <p>24 applications is being compared against that</p> <p>25 population that still had no applications in it.</p>

<p style="text-align: right;">Page 302</p> <p>1 So that odds ratio for that first dosing</p> <p>2 is influenced by the never-users still being</p> <p>3 contained in that grouping.</p> <p>4 Q You're speculating, aren't you, that</p> <p>5 those odds ratios are influenced by the never-users?</p> <p>6 MS. CURRY: Object to the form.</p> <p>7 THE WITNESS: No --</p> <p>8 BY MS. GARBER:</p> <p>9 Q You have no data to suggest that that has</p> <p>10 positively influenced the data, do you?</p> <p>11 MS. CURRY: Object to the form.</p> <p>12 THE WITNESS: I absolutely do. That's</p> <p>13 actually how Terry calculated their dose response.</p> <p>14 They pulled the never-users out, and they commented</p> <p>15 that this is the only way to actually go look for a</p> <p>16 dose response. Your never-users are not going to</p> <p>17 have a statistically significant increased risk</p> <p>18 because they have no applications.</p> <p>19 So their referent number is one. That's</p> <p>20 a lower number by the fact that they're never-users.</p> <p>21 Terry pulled those patients out, the never-users,</p> <p>22 when Terry went about doing the dose calculations.</p> <p>23 And Terry did not find a statistically significant</p> <p>24 dose response curve.</p> <p>25 ///</p>	<p style="text-align: right;">Page 304</p> <p>1 actually the entire issue of recall bias. Any case</p> <p>2 control studies is up and open to recall bias. I</p> <p>3 have no reason to believe that somebody would report</p> <p>4 they never used talc if they never used it. But I</p> <p>5 don't have actual data on that.</p> <p>6 Q Do you have an opinion that recall bias</p> <p>7 accounts for the positive association in the case</p> <p>8 control studies?</p> <p>9 MS. CURRY: Object to the form.</p> <p>10 THE WITNESS: I think it has the</p> <p>11 potential to contribute to it.</p> <p>12 BY MS. GARBER:</p> <p>13 Q But that's not my question. Do you think</p> <p>14 that the positive results, the statistically</p> <p>15 significant association in the case control studies</p> <p>16 are attributable to recall bias?</p> <p>17 MS. CURRY: Object to the form.</p> <p>18 THE WITNESS: Not exclusively, but I</p> <p>19 think there is the potential that recall bias is</p> <p>20 influencing the odds ratios in the case control</p> <p>21 studies along with other factors that case control</p> <p>22 studies are subject to.</p> <p>23 BY MS. GARBER:</p> <p>24 Q So I'm here to get your opinion. So</p> <p>25 there's potential, but it is not your opinion that</p>
<p style="text-align: right;">Page 303</p> <p>1 BY MS. GARBER:</p> <p>2 Q Are there other data that support that</p> <p>3 failure to pull out the never-users inflated the</p> <p>4 odds ratio?</p> <p>5 MS. CURRY: Object to the form.</p> <p>6 THE WITNESS: No, every other study left</p> <p>7 them in. That's not the proper way to do that</p> <p>8 analysis, because you're weighting your lower</p> <p>9 applications by the never-users. They don't belong</p> <p>10 in the dose response calculations, because they</p> <p>11 don't have applications.</p> <p>12 BY MS. GARBER:</p> <p>13 Q But you don't know the way that you just</p> <p>14 cited in Terry in the other studies that the</p> <p>15 never-users affected the results, do you?</p> <p>16 MS. CURRY: Object to the form.</p> <p>17 THE WITNESS: No, I do, because they have</p> <p>18 an odds ratio, a referent value of one. So that is</p> <p>19 the referent value because they have no exposures.</p> <p>20 That's influencing the lower dose applications.</p> <p>21 BY MS. GARBER:</p> <p>22 Q Do you have any data to indicate that the</p> <p>23 study subjects that reported no use did, in fact,</p> <p>24 have no use?</p> <p>25 A So I think what you're getting at is</p>	<p style="text-align: right;">Page 305</p> <p>1 those studies are, in fact, influenced by recall</p> <p>2 bias; correct?</p> <p>3 A I do --</p> <p>4 MS. CURRY: Object to the form.</p> <p>5 THE WITNESS: I do believe that</p> <p>6 Schildkraut demonstrated that recall bias</p> <p>7 contributes to the odds ratio because when</p> <p>8 Schildkraut analyzed the data pre-2014 and</p> <p>9 post-2014, the odds ratio changed. So I do believe</p> <p>10 that as a piece of data, the Schildkraut study does</p> <p>11 show the influence of recall bias in case control</p> <p>12 studies -- sorry, in her study.</p> <p>13 BY MS. GARBER:</p> <p>14 Q Do you know when there was the first</p> <p>15 widespread coverage or media coverage of the talcum</p> <p>16 powder litigation?</p> <p>17 MS. CURRY: Object to the form.</p> <p>18 THE WITNESS: No, I do not.</p> <p>19 BY MS. GARBER:</p> <p>20 Q Did you read any studies that talked</p> <p>21 about that?</p> <p>22 A About the recall bias?</p> <p>23 Q Uh-huh.</p> <p>24 A Or the litigation?</p> <p>25 Q Uh-huh.</p>

<p style="text-align: right;">Page 306</p> <p>1 A Other than Schildkraut?</p> <p>2 Q Uh-huh.</p> <p>3 A Penninkilampi talks about it.</p> <p>4 Q We'll get to some of that in a minute.</p> <p>5 Do you have an opinion about whether the</p> <p>6 epidemiological data provides consistent increased</p> <p>7 risk of ovarian cancer?</p> <p>8 MS. CURRY: Object to the form.</p> <p>9 THE WITNESS: I'm sorry, you're going to</p> <p>10 have to rephrase that. That's really broad. The</p> <p>11 epidemiologic literature shows increased risk of</p> <p>12 ovarian cancer?</p> <p>13 MS. GARBER: Yes.</p> <p>14 THE WITNESS: That's very broad. I</p> <p>15 don't -- can you please rephrase that?</p> <p>16 BY MS. GARBER:</p> <p>17 Q What are your opinions about whether or</p> <p>18 not the epidemiological data is -- provides</p> <p>19 consistency or inconsistency? Don't you have</p> <p>20 opinions about that in your report?</p> <p>21 MS. CURRY: Object to the form.</p> <p>22 THE WITNESS: With respect to what and</p> <p>23 what?</p> <p>24 BY MS. GARBER:</p> <p>25 Q With respect to genital talc use and risk</p>	<p style="text-align: right;">Page 308</p> <p>1 Do you see where I am?</p> <p>2 A So the -- is this the synopsis section?</p> <p>3 Q Yes. Do you see at the bottom of -- the</p> <p>4 third page in, under the synopsis, the second to the</p> <p>5 last paragraph?</p> <p>6 A Yes.</p> <p>7 Q It reads, "The meta-analyses of the</p> <p>8 available human studies and peer-reviewed literature</p> <p>9 indicate a consistent and statistically significant</p> <p>10 positive association between perineal exposure to</p> <p>11 talc in ovarian cancer."</p> <p>12 Do you disagree with that statement of</p> <p>13 these authors who drafted this for Health Canada?</p> <p>14 A Yes, the literature is not consistent.</p> <p>15 In fact, Berge talks about that. There's</p> <p>16 heterogeneity between case control studies and the</p> <p>17 cohort studies.</p> <p>18 Q So here, again, you're disagreeing with</p> <p>19 authors who have actually performed an analysis of</p> <p>20 the data.</p> <p>21 MS. CURRY: Object to the form.</p> <p>22 THE WITNESS: These authors didn't</p> <p>23 perform an analysis. This is a draft screening</p> <p>24 assessment, and in fact, I'm very consistent with</p> <p>25 what Berge puts forth, which is that there's</p>
<p style="text-align: right;">Page 307</p> <p>1 of ovarian cancer.</p> <p>2 A I think the epidemiologic literature on</p> <p>3 the risk of -- the possible risk of perineal</p> <p>4 application of talc and the development of ovarian</p> <p>5 cancer is inconsistent.</p> <p>6 Q You're aware of study data that</p> <p>7 indicate -- strike that.</p> <p>8 You're aware of study authors in</p> <p>9 epidemiological studies that indicate that the</p> <p>10 literature is consistent, not inconsistent; correct?</p> <p>11 MS. CURRY: Object to the form.</p> <p>12 THE WITNESS: No, you'd have to point me</p> <p>13 to what exactly you're referencing.</p> <p>14 MS. GARBER: Let's go back to Health</p> <p>15 Canada, which is Exhibit 20.</p> <p>16 THE WITNESS: Okay.</p> <p>17 MS. CURRY: Exhibit 19?</p> <p>18 MS. GARBER: Is it 19?</p> <p>19 THE WITNESS: Yes.</p> <p>20 MS. GARBER: Thank you. I misspoke. So</p> <p>21 Exhibit 19, that draft screening assessment of</p> <p>22 Health Canada.</p> <p>23 BY MS. GARBER:</p> <p>24 Q Could you please turn to page -- it's not</p> <p>25 three, but it's Roman three. It's three pages in.</p>	<p style="text-align: right;">Page 309</p> <p>1 heterogeneity, meaning inconsistency, between the</p> <p>2 cohort studies and the case control studies.</p> <p>3 MS. GARBER: Let's mark the Taher study.</p> <p>4 THE REPORTER: Which study?</p> <p>5 MS. GARBER: T-A-H-E-R, 2018. I'm going</p> <p>6 to mark as Exhibit 29 the Taher 2018 meta-analysis.</p> <p>7 (C. Saenz Exhibit 29 was marked for</p> <p>8 identification.)</p> <p>9 THE WITNESS: Thank you.</p> <p>10 BY MS. GARBER:</p> <p>11 Q Could you please turn to page 49 of the</p> <p>12 study. Under the conclusion section, beginning with</p> <p>13 "consistent," the authors conclude "Consistent with</p> <p>14 previous evaluations, the IARC and subsequent</p> <p>15 evaluations by individual investigators, the present</p> <p>16 comprehensive evaluation of all currently available</p> <p>17 relevant data indicates that perineal exposure to</p> <p>18 talcum powder is a possible cause of ovarian cancer</p> <p>19 in humans."</p> <p>20 I'm assuming that you disagree with that</p> <p>21 conclusion.</p> <p>22 A I disagree with that. I mean, they are</p> <p>23 basically saying what IARC said, and I disagree with</p> <p>24 that.</p> <p>25 Q You disagree that the literature is</p>

<p style="text-align: right;">Page 310</p> <p>1 consistent?</p> <p>2 A I disagree that the literature is</p> <p>3 consistent, because again the cohort studies do not</p> <p>4 show an increased risk.</p> <p>5 Q And you disagree that the perineal</p> <p>6 exposure to talc is a possible cause of ovarian</p> <p>7 cancer in humans?</p> <p>8 A Yes.</p> <p>9 Q Turning back to the Terry 2013 paper. If</p> <p>10 you turn to page six of that study where it</p> <p>11 indicates "Based on the consistency," do you see</p> <p>12 that?</p> <p>13 A I'm sorry, where are we?</p> <p>14 Q If you could hand that to me, because I</p> <p>15 can't find mine. Thanks.</p> <p>16 A No problem.</p> <p>17 Q Thank you. Page six, under the</p> <p>18 discussion. Do you see where it begins, "Based on</p> <p>19 the consistency"?</p> <p>20 A Yes.</p> <p>21 Q It reads, "Based on the consistency of</p> <p>22 the epidemiologic literature on talc-based body</p> <p>23 powder and ovarian cancer risk, the IARC classified</p> <p>24 talc-based body powder as a 2(b) carcinogen,</p> <p>25 possibly carcinogenic in human beings."</p>	<p style="text-align: right;">Page 312</p> <p>1 BY MS. GARBER:</p> <p>2 Q In your report at page eight, under the</p> <p>3 heading, "Genital Application of Talc," you</p> <p>4 indicate, "The majority of the published studies" --</p> <p>5 A I'm sorry. Give me a second. I see</p> <p>6 where you are, yes.</p> <p>7 Q "The majority of the published studies</p> <p>8 consist of small, retrospective case control studies</p> <p>9 with inherent selection and recall bias."</p> <p>10 A Biases.</p> <p>11 Q Biases.</p> <p>12 A Yes.</p> <p>13 Q That's your opinion?</p> <p>14 A Yes.</p> <p>15 Q The majority of them?</p> <p>16 A Yes.</p> <p>17 Q Okay. Are you aware of study author</p> <p>18 statements that have indicated that those data are</p> <p>19 not subject to recall bias?</p> <p>20 MS. CURRY: Object to the form.</p> <p>21 THE WITNESS: No, you would have to show</p> <p>22 me that, and I don't believe that you can entirely</p> <p>23 eliminate recall bias from a case control study.</p> <p>24 And selection bias is always going to be a component</p> <p>25 of a case control study because you will have people</p>
<p style="text-align: right;">Page 311</p> <p>1 So there the Terry papers are citing to</p> <p>2 IARC, where IARC was saying the data are consistent;</p> <p>3 correct?</p> <p>4 A So Terry is citing IARC, which is a 2010</p> <p>5 publication, and that's before the cohort studies</p> <p>6 such as when the talc initiative study was</p> <p>7 published. So IARC didn't actually analyze those</p> <p>8 studies, and I do believe that here, Terry is simply</p> <p>9 quoting what IARC has to say.</p> <p>10 Q Okay. Did you consider the -- did you</p> <p>11 consider the issue of recall bias in formulating</p> <p>12 your opinions in this case?</p> <p>13 MS. CURRY: Object to the form.</p> <p>14 THE WITNESS: With respect to what?</p> <p>15 BY MS. GARBER:</p> <p>16 Q With regard to the sufficiency of the</p> <p>17 literature and what it showed.</p> <p>18 MS. CURRY: Object to the form.</p> <p>19 THE WITNESS: I think recall bias is</p> <p>20 always an issue. Whenever there's a case control</p> <p>21 study, I don't think that that's something that you</p> <p>22 can necessarily eliminate. You can try and control</p> <p>23 for it, but as we discussed earlier and as evidenced</p> <p>24 by the Schildkraut study, there's certainly an</p> <p>25 influence of, on the odds ratios, of recall bias.</p>	<p style="text-align: right;">Page 313</p> <p>1 that don't participate in terms of who your cases</p> <p>2 are. And what is the reason for them to not</p> <p>3 participate and the people that do participate, to</p> <p>4 participate, you can't sort out. You don't know</p> <p>5 what those influences are.</p> <p>6 BY MS. GARBER:</p> <p>7 Q At Exhibit 19, page 28.</p> <p>8 A What document are we on now, ma'am?</p> <p>9 Q Sorry, the Health Canada.</p> <p>10 A Health Canada.</p> <p>11 Q Health Canada, page 28.</p> <p>12 A Okay.</p> <p>13 Q Under the heading, "Uncertainties in the</p> <p>14 Evaluation of Risk in Human Health," third paragraph</p> <p>15 down, beginning with the sentence, "However."</p> <p>16 Do you see where I am?</p> <p>17 A Yes.</p> <p>18 Q The next sentence down, it begins, "The</p> <p>19 studies where the exposure is simple, e.g., never</p> <p>20 versus ever use, recall bias is unlikely to be an</p> <p>21 important source of bias."</p> <p>22 Then it cites to Narod 2016. "The</p> <p>23 positive association is strongest for serous</p> <p>24 histologic type." Then he cites to Berge 2018.</p> <p>25 Taher, 2018. "The findings that the association may</p>

<p style="text-align: right;">Page 314</p> <p>1 vary by histologic type detracts from the hypothesis 2 of report bias, as this type of bias would likely 3 operate in all histologic types." 4 Then he cites to the Berge 2018 paper. 5 Correct? 6 A That's what it says there, but that's 7 just not true. 8 Q So let's talk about that for a minute. 9 If recall bias were at play, then it wouldn't 10 operate in some histologies and not others, would 11 it? 12 A So the studies that have shown the 13 association with the serous subtype was the Gertig 14 2000 study, which in the follow-up study with Gates 15 in 2010, did not show the association with the 16 serous subtype. 17 Q Were there other studies that you saw 18 where serous subtype was more highly associated with 19 risk of ovarian cancer than the other subtypes? 20 A So across the different literature that 21 has been published at various times, there has been 22 association with the serous type, but there have 23 also been associations with the endometrial type. 24 So the literature has varied, according to what 25 subtypes were found.</p>	<p style="text-align: right;">Page 316</p> <p>1 A Yes. 2 Q It reads: "Methodological factors such 3 as recall bias could always be considered in case 4 control studies." 5 MS. CURRY: Should always be considered. 6 MS. GARBER: "It could have been a 7 problem had there been widespread publicity about 8 the possible association between use of body powder 9 and cancer. The International Agency For Research 10 on Cancer, IARC, working group, considers that there 11 has not been widespread public concern about this 12 issue, and therefore, considers it unlikely that 13 such bias could play -- could explain the consistent 14 findings." 15 BY MS. GARBER: 16 Q Did I read that correctly? 17 A Yes, and it goes on, "Another source of 18 recall bias could result from the fact that women 19 with cancer tend to remember or overreport their use 20 of body powder," which is exactly what I was saying 21 before. 22 Q Isn't it true, Doctor, that habitual use 23 eliminates or reduces the risk of recall bias? 24 MS. CURRY: Object to the form. 25 THE WITNESS: It can reduce recall bias,</p>
<p style="text-align: right;">Page 315</p> <p>1 I also think, again, I would cite back to 2 Schildkraut, which demonstrated the influence of 3 recall bias, regardless. And I just don't think 4 that you can completely eliminate recall bias. 5 You're talking about patients with 6 ovarian cancer that are searching for answers as to 7 why they got their disease. They want to know why 8 they're in this unfortunately circumstance, and we 9 don't really know how the people that were doing the 10 questions were asking them the questions and how 11 that might influence them as well. 12 Q Can you pull the Langseth paper from 13 2008. 14 MS. CURRY: Which exhibit number was 15 that? 16 MS. GARBER: I think it was seven. 17 MS. THOMPSON: It's 12. 18 MS. GARBER: It was not. It was 12. 19 THE WITNESS: Almost there. 20 BY MS. GARBER: 21 Q If you turn to page 358. 22 A Is that the first page? 23 Q Yeah. On the right-hand column, the 24 paragraph that begins with "Methodological factors," 25 do you see that?</p>	<p style="text-align: right;">Page 317</p> <p>1 but you can't eliminate it. And even as the authors 2 say in this paper that you were just reading from, 3 the influence of this type of recall bias cannot be 4 ruled out. So habitual use doesn't even rule out 5 the possibility that the women with cancer tend to 6 overreport or remember more so their use of body 7 powder. 8 BY MS. GARBER: 9 Q Would you read the Narod 2016 publication 10 with regard to talc in ovarian cancer. I didn't see 11 it cited on your reference list. 12 A I think in the course of being a GYN 13 oncologist, I probably read it, but I don't know 14 that I read it specifically for the purposes of 15 generating my report. 16 MS. GARBER: So I've marked that as 17 Exhibit 30. 18 (C. Saenz Exhibit 30 was marked for 19 identification.) 20 BY MS. GARBER: 21 Q Doctor, this was published in Gynecologic 22 Oncology, so this is something that you probably 23 would have read? 24 A Quite possibly; yes. 25 Q Doctor, here, Dr. Narod discusses that</p>

<p style="text-align: right;">Page 318</p> <p>1 case control studies to date are consistent on the 2 right-hand column, doesn't he? 3 A He writes, "The case control studies to 4 date are consistent," yes. 5 Q If you turn -- 6 A He goes on to say, "Given the small 7 effect size, it is not surprising that some are 8 positive and some are negative." 9 Q Does he also discuss the cohort studies, 10 if you turn the page over in the left-hand column, 11 about halfway down, beginning with the word 12 "neither"? 13 MS. CURRY: I don't see where you are. 14 THE WITNESS: I don't either. 15 MS. GARBER: Second page in. 16 THE WITNESS: Yes, ma'am. 17 MS. GARBER: Left-hand column. 18 THE WITNESS: Yes, ma'am. 19 MS. GARBER: About halfway down the 20 paragraph, right after the odds ratio that ends with 21 the competence interval of 1.15. 22 THE WITNESS: I'm sorry, say that number 23 again. 24 MS. GARBER: Let me show you, where it 25 says "neither."</p>	<p style="text-align: right;">Page 320</p> <p>1 meta-analysis, when Berge looked at the cohort 2 studies and put them together, Berge did a 3 mathematical calculation to look at the power of the 4 cohort studies to be able to detect a relative risk 5 of 1.25. 6 And what Berge found was that when you 7 put the cohort studies together, you actually do 8 achieve the statistical significance to detect a 9 relative risk of 1.25 to the 99th percentile. 10 So the power is actually there within the 11 cohort studies, particularly when you do a 12 meta-analysis with them. 13 So I disagree that that data is not 14 available. I think that this is why Berge came to 15 the conclusion that you cannot say the heterogeneity 16 between the case control studies and the cohort 17 studies is due to the cohort studies lacking power. 18 BY MS. GARBER: 19 Q None of the cohort studies have a study 20 population of 200,000 women, do they? 21 MS. CURRY: Object to the form. 22 THE WITNESS: No, they don't, but the 23 pool of them does. And the pool of them did not 24 detect a statistically significant difference in the 25 risk of developing ovarian cancer with the use of</p>
<p style="text-align: right;">Page 319</p> <p>1 THE WITNESS: Thank you; okay. 2 BY MS. GARBER: 3 Q It indicates: "Neither prospective study 4 confirmed the association of talc use in ovarian 5 cancer raised by the case control studies, but 6 neither study was powered to detect the risk of 1.2 7 and, therefore, we cannot exclude the possibility." 8 He goes on to say, "Only two women in a 9 thousand will develop ovarian cancer in ten-year 10 follow-up period. If we study 10,000 women over ten 11 years, we can expect 20 cancers to occur. If the 12 true odds ratio is 1.2, we will expect 20 cancers in 13 the unexposed group of 100,000." 14 MS. CURRY: 10,000. 15 THE WITNESS: 10,000. 16 BY MS. GARBER: 17 Q And so on. He goes on to say, "In order 18 to achieve statistical significance in the 19 prospective study, we would need a much larger 20 cohort, e.g., we would need a study upwards of 21 200,000 women for ten years?" 22 Did I read that correctly? 23 A So, one, he does say that. Two, I don't 24 know what his -- the bases for his calculations and, 25 three, we actually do have that data. Berge in the</p>	<p style="text-align: right;">Page 321</p> <p>1 perineal talc. 2 BY MS. GARBER: 3 Q What did the Penninkilampi data find with 4 regard to the cohort studies? 5 MS. CURRY: Object to the form. 6 THE WITNESS: So the Penninkilampi study 7 only looked -- 8 MS. GARBER: Go ahead, I'm sorry. 9 THE WITNESS: That's okay. 10 BY MS. GARBER: 11 Q The Penninkilampi study only looked at 12 the Gertig data. It didn't look at the Gates data. 13 Do you take issue with that? 14 A I do. 15 Q Why? 16 A Because I would think that study authors 17 that are trying to conduct a meta-analysis would 18 always want to look at the most mature data, 19 particularly in cohort study. So I understand that 20 the authors didn't -- 21 Q I'm listening. I promise you, I'm 22 listening. I'm sorry. We're just short on time. I 23 can do two things at once. I'm a woman. 24 A Understood. I understand that 25 Penninkilampi didn't want to have duplicate data.</p>

<p style="text-align: right;">Page 322</p> <p>1 Q Okay; yes.</p> <p>2 A I understand that Penninkilampi didn't</p> <p>3 want to have duplicate data, so they said they</p> <p>4 didn't want to reanalyze the same patient study</p> <p>5 population. But I still -- can you move that water</p> <p>6 bottle? Sorry. This one. The light is reflecting</p> <p>7 off of it. Thank you so much.</p> <p>8 But that means that they should have</p> <p>9 favored an analysis of the Gates data over the</p> <p>10 Gertig data and they did not.</p> <p>11 Q Do you know what the metric of exposure</p> <p>12 was for the Penninkilampi meta-analysis?</p> <p>13 MS. CURRY: Object to the form.</p> <p>14 THE WITNESS: You mean what did they</p> <p>15 calculate their odds ratio off of?</p> <p>16 BY MS. GARBER:</p> <p>17 Q How did they select the exposure for</p> <p>18 purposes of their meta-analysis that was conducted?</p> <p>19 A I'd have to go look at the original study</p> <p>20 again. I can't recall off the top of my head.</p> <p>21 MS. GARBER: Let's mark Exhibit 31 the</p> <p>22 Penninkilampi study.</p> <p>23 (C. Saenz Exhibit 31 was marked for</p> <p>24 identification.)</p> <p>25 ///</p>	<p style="text-align: right;">Page 324</p> <p>1 data; correct?</p> <p>2 A Well, they didn't include the Gates data.</p> <p>3 It's not that they included the Gertig data that I</p> <p>4 take issue with. It's that they didn't include the</p> <p>5 Gates data.</p> <p>6 MS. GARBER: Now, if I mark Gertig, as</p> <p>7 Exhibit 32.</p> <p>8 (C. Saenz Exhibit 32 was marked for</p> <p>9 identification.)</p> <p>10 BY MS. GARBER:</p> <p>11 Q Doctor, if we turn to the Gertig data</p> <p>12 that the Penninkilampi authors included, was an odds</p> <p>13 ratio of 1.09, with a confidence interval of .86 to</p> <p>14 1.38; is that correct?</p> <p>15 A I'm looking at the Penninkilampi table.</p> <p>16 Do you want to reference me where to look in the</p> <p>17 Gertig paper?</p> <p>18 Q I do. So let's do this together. So in</p> <p>19 the Penninkilampi publication, under --</p> <p>20 A Table A, yes.</p> <p>21 Q -- figure 2(a) --</p> <p>22 A Right.</p> <p>23 Q -- the Gertig data that's reported, is an</p> <p>24 odds ratio of 1.09, .86 to 1.38; correct?</p> <p>25 A Yes.</p>
<p style="text-align: right;">Page 323</p> <p>1 BY MS. GARBER:</p> <p>2 Q Doctor, if you look at table two, sorry.</p> <p>3 If you look at figure two at page 46. Do you see</p> <p>4 for figure 2(a), the metric is ever-talc use or</p> <p>5 any-talc use?</p> <p>6 A I'm sorry, where are you?</p> <p>7 Q Under figure two.</p> <p>8 A Are we reading the legend?</p> <p>9 Q Yes.</p> <p>10 A Thank you.</p> <p>11 Q Figure 2(a), it indicates, "Any perineal</p> <p>12 talc use is associated with an increased risk";</p> <p>13 right?</p> <p>14 A Yes.</p> <p>15 Q Figure 2(a), the metric, is ever-use of</p> <p>16 talc; correct?</p> <p>17 A Well, it says "Any perineal talc use";</p> <p>18 yes.</p> <p>19 Q Ever-use; right?</p> <p>20 A I don't see where it says "ever."</p> <p>21 Q Well, any, ever, those are used</p> <p>22 interchangeably, aren't they?</p> <p>23 A Fair enough.</p> <p>24 Q So now if we go -- you take issue because</p> <p>25 the Penninkilampi authors included the Gertig 2000</p>	<p style="text-align: right;">Page 325</p> <p>1 Q We've already established that this is</p> <p>2 for ever-use of talc; right?</p> <p>3 A That's what the legend says.</p> <p>4 Q Now, if we go over to table two in the</p> <p>5 Gertig paper and we see ever-use of talc, we see</p> <p>6 that that's where the Penninkilampi authors got</p> <p>7 their data; correct?</p> <p>8 A So the adjusted odds ratio is 1.09 with</p> <p>9 0.86 to 1.37; correct.</p> <p>10 Q Okay. So --</p> <p>11 A So that's not exactly the same.</p> <p>12 Q Well, it's off by --</p> <p>13 A By .01.</p> <p>14 Q Close enough?</p> <p>15 A I guess for government work. But it's</p> <p>16 not exactly the same.</p> <p>17 Q For epidemiologic work. Now, if we go to</p> <p>18 the Gates paper, I'll mark that as Exhibit 33.</p> <p>19 (C. Saenz Exhibit 33 was marked for</p> <p>20 identification.)</p> <p>21 BY MS. GARBER:</p> <p>22 Q And we turn to table one at the Gates</p> <p>23 2010 paper, the authors reported that genital talc</p> <p>24 use by way of frequency; correct, not ever-never?</p> <p>25 A Correct.</p>

<p style="text-align: right;">Page 326</p> <p>1 Q So it would have been incorrect of the 2 Penninkilampi authors to include the Gates data, 3 because between the Gertig data, looking at 4 ever-never, the Gates data presented only a 5 frequency of use, so that would be comparing apples 6 to oranges by way of exposure, wouldn't it, Doctor? 7 MS. CURRY: Object to the form. 8 THE WITNESS: By that analysis, then, 9 Penninkilampi also should not have included Wu 2015. 10 Because Wu 2015 included in its analysis as 11 never-users anybody that reported use of less than 12 one year. 13 So it wasn't pure, and yet, they included 14 Wu 2015 in the analysis for the same rationale that 15 you've just pointed out Gates. 16 So Wu 2015 is in figure 2(a). So if the 17 authors are really trying to pull out and only 18 report on ever-never users, then Wu 2015 should not 19 have been included in the analysis either. 20 BY MS. GARBER: 21 Q Well, Wu -- did Wu 2009 provide 22 ever-never? 23 A That's -- 24 MS. CURRY: Object to the form. 25 THE WITNESS: -- not the issue. The</p>	<p style="text-align: right;">Page 328</p> <p>1 BY MS. GARBER: 2 Q Have you analyzed the Berge data to see 3 if the consistency of the exposures are consistent 4 throughout the meta-analysis data? 5 MS. CURRY: Object to the form. 6 THE WITNESS: Berge 2015 didn't make an 7 exclusion based on that. What I'm saying is that I 8 think you would always want to report on a study 9 that has longer latency to -- especially when you're 10 looking at development of a cancer. And Gates has a 11 longer latency than Gertig. 12 Within Wu 2015, there were patients that 13 had exposure that were grouped in never-users. So I 14 don't think that that's a reason to eliminate the 15 Gates study. 16 BY MS. GARBER: 17 Q Do you -- and I don't know why the 18 authors relied on the Gates -- on the Gertig versus 19 the Gates, because it's not in the paper. Do you? 20 A No, that's true. I tried to figure that 21 out as well by thoroughly reading that paper. What 22 I do know is that they said they -- within their 23 methodology section, that they didn't include 24 studies that had patients that were previously 25 reported on.</p>
<p style="text-align: right;">Page 327</p> <p>1 issue is, you're trying to explain that Gertig was 2 included and Gates wasn't, because it was an 3 ever-never use reporting. And what I'm saying is, 4 in figure 2(a), the fourth study down, Wu 2015 are 5 was not an ever-never use reporting. 6 So if the reason Gates was left out is 7 because frequency of use of, what was it, less than 8 one time per week was the report, then Wu 2015 9 should have been left out as well. Because Wu 2015 10 grouped women that used talc, but reported less than 11 one year of use, in with the never-users. 12 BY MS. GARBER: 13 Q Do you think in your experience, which 14 doesn't include a degree in epidemiology, that it 15 was improper for the Penninkilampi authors to 16 analyze the Gertig 2000 data rather than the Gates 17 2010 data? 18 MS. CURRY: Object to the form. 19 THE WITNESS: Yes, I do. And if the 20 rash -- especially in the rationale that you're 21 trying to propose is because they're trying to be 22 pure in the reporting of ever-never data, then they 23 weren't. Wu 2015 does not belong in that analysis 24 if the rationale that you're proposing is actually 25 what they did.</p>	<p style="text-align: right;">Page 329</p> <p>1 Q Let's talk about some of the cohorts 2 quickly, and then we'll move on to a final area -- 3 A Sure. 4 Q -- before my time expires. So in the 5 three cohort studies that you looked at, the Nurses 6 Health Study, the W-H-I and the sister study, did 7 those support your opinion that there's no credible 8 scientific evidence that talc increases risk for 9 developing ovarian cancer? 10 MS. CURRY: Object to the form. 11 THE WITNESS: They helped form my 12 opinion. 13 BY MS. GARBER: 14 Q So where the other studies were not 15 credible, these studies were? 16 MS. CURRY: Object to the form. 17 THE WITNESS: No, that's not what I said. 18 I've read everything that's there and analyzed 19 everything that I've read and every single study 20 that I've read has helped to influence my opinion. 21 I've come to the conclusions that I've 22 come to, because I've read all of these studies. So 23 just because they didn't have a statistically 24 significant finding or just because the data was 25 inconsistent doesn't mean I discounted that</p>

<p style="text-align: right;">Page 330</p> <p>1 literature. I actually evaluated that in terms of 2 generating my opinion. 3 BY MS. GARBER: 4 Q Doctor, you make reference at page 30 of 5 your report to junk science. Which of the 6 peer-reviewed public -- published data is junk 7 science that you're referencing? 8 MS. CURRY: Object to the form. 9 THE WITNESS: I'm not referencing any one 10 particular manuscript or article. I'm just saying 11 the supposition that talc causes ovarian cancer is 12 junk science. 13 BY MS. GARBER: 14 Q So the literature which supports that 15 talc is associated with a statistically significant 16 increased risk of epithelial ovarian cancer is junk 17 science? 18 MS. CURRY: Object to the form. 19 THE WITNESS: The hypothesis is. It's 20 not supported by the science. 21 BY MS. GARBER: 22 Q With regard to the cohort studies, let's 23 turn to the Gates 2010 study. That was a follow-up 24 of the Gertig 2000 study; correct? 25 MS. CURRY: Do you have another copy?</p>	<p style="text-align: right;">Page 332</p> <p>1 BY MS. GARBER: 2 Q The cohort studies were reliable based on 3 a couple of factors, one of the which is that the 4 women were the right age. 5 MS. CURRY: Object to the form. 6 BY MS. GARBER: 7 Q Is that correct? 8 A Can you direct me to the page in my 9 report that we're discussing? 10 Q Page 13. Let's turn specifically to the 11 Gates study. The age of the women in the Gates 12 study were 25 to 42; correct? 13 A Not at enrollment. 14 Q In the Gates study, the study did not ask 15 the question about talc. Instead, it just carried 16 forward the data from the Gertig, one time, 1982 17 questionnaire; is that correct? 18 A So at enrollment, so the Gates study had 19 two components. The NHS-1 Group of patients that 20 were actually originally enrolled and asked about 21 talc in 1982. And the women in that analysis 22 were -- I'm trying to find the information on age at 23 the time of enrollment. 24 Q Doctor, in the Gertig study, the women at 25 the time of enrollment were age 30 to 55.</p>
<p style="text-align: right;">Page 331</p> <p>1 This is the wrong publication. 2 THE WITNESS: It's this one. 3 MS. CURRY: I know, that's what I'm 4 looking for. 5 MS. GARBER: It's just a different -- 6 it's the same publication. 7 MS. CURRY: No, no, it's not. This is a 8 different article. 9 THE WITNESS: This is the 2008. This is 10 the 2010. 11 MS. GARBER: They got merged again. 12 Sorry. Maybe she can pull one out. 13 BY MS. GARBER: 14 Q So does the Gates article, it's follow-up 15 to the Gertig 2000 paper; correct? 16 A I mean, with respect to the NHS-1 study; 17 yes. 18 Q And you indicate that the case control 19 studies were reliable based on a couple of factors, 20 one, that the women were the right study population; 21 correct? 22 MS. CURRY: Object to the form. 23 THE WITNESS: You just said "case control 24 studies." No, that's actually not true. 25 ///</p>	<p style="text-align: right;">Page 333</p> <p>1 A Right. So that's not the number that you 2 just quoted me. So at the time of enrollment in the 3 Gertig study, they were 30 to 55; correct. 4 Q They were followed for 14 years; correct? 5 MS. CURRY: Object to the form. 6 THE WITNESS: That's how old they were 7 when they enrolled in 1976. They were asked the 8 question about talc in 1982. So they actually would 9 be six years older when they were asked about talc 10 and then they were followed for 14 years. 11 BY MS. GARBER: 12 Q When you say at page 14 that based on the 13 use of, that the average use is greater than 14 20 years, based on the Wu 2015 data, you're 15 speculating -- 16 A Where -- 17 Q -- as to when it stopped. In your expert 18 report. 19 A Page 14? 20 Q You indicate a criticism is often made of 21 the two studies, that they were only -- that they 22 only ascertained information on talc usage at one 23 point. But we know from Wu 2015, however, the women 24 who are ever users of talc in perineal area, the 25 mean duration of use is 20 years.</p>

<p style="text-align: right;">Page 334</p> <p>1 So you're speculating about the years of 2 talc use, based on the Wu data; correct? 3 MS. CURRY: Object to the form. 4 BY MS. GARBER: 5 Q You don't know that, you don't have any 6 firsthand knowledge, do you? 7 MS. CURRY: Object to the form. 8 THE WITNESS: Well, of course, I don't 9 have firsthand knowledge, but I'm building upon what 10 Wu published. And what Wu published is that the 11 average of duration of use of women that are talc 12 users is more than 20 years. 13 BY MS. GARBER: 14 Q But you're speculating -- 15 A I have no reason to believe that the 16 population in either Gertig or Gates is not typical 17 of the same population that Wu studied. 18 Q But you don't have any reason to know 19 that it was. This is an entire different study, 20 cohort, than the Wu data, wasn't it? 21 MS. CURRY: Object to form. 22 THE WITNESS: It's a different study, but 23 the women are talc users and there's every reason to 24 believe that a talc user is a talc user and the 25 duration of use is going to be more than 20 years.</p>	<p style="text-align: right;">Page 336</p> <p>1 to capture a 30- or 40-year latency for ovarian 2 cancer, were they? 3 MS. CURRY: Objection to form. 4 THE WITNESS: I disagree with that. I 5 think that in particular, with Gates and Gertig 6 study, the length of study time in that study was 7 24 years. The length of study in that study for 8 follow-up was 24 years, and if we then look at as 9 reported by Wu and as reported by Dr. Cramer, these 10 women most likely started by their mid 20s and had 11 used for more than 30 years then -- I'm sorry, more 12 than 20 years, then we actually are in the range of 13 30 plus years of latency. 14 BY MS. GARBER: 15 Q But, Doctor, to make that statement, 16 you're speculating. You don't have any information 17 from the studies that support the length of use, do 18 you? 19 A That's actually not true. The women's 20 health initiative study reported on women that had 21 used talc for more than 20 years. It then followed 22 women for 12.4 years. That puts us at 32.4 years. 23 So if you ask me whether or not the 24 latency ever got to 30 years, absolutely it did. At 25 a minimum for the women that reported more than</p>
<p style="text-align: right;">Page 335</p> <p>1 BY MS. GARBER: 2 Q The study does not give that information, 3 does it? 4 A The study doesn't include that 5 information. 6 Q Also, the Houghton study does not give 7 that information, does it? 8 MS. CURRY: Object to the form. 9 THE WITNESS: That's actually not true. 10 The Houghton study actually did study women who 11 reported on more than 20 years of usage. Houghton 12 looked at duration. 13 BY MS. GARBER: 14 Q The Gonzalez sister study did not 15 indicate the years of use, did it? 16 A That's correct. 17 Q There again, like Gates, you relied on 18 extrapolation from the Cramer study to give you that 19 data; correct? 20 A I relied on the data as reported by 21 Dr. Cramer as to the age at which women start using, 22 but I also relied on IARC, even though I don't quote 23 it there, because IARC talks about women that are 24 talc users usually starting by their mid 20s. 25 Q These cohort studies were not long enough</p>	<p style="text-align: right;">Page 337</p> <p>1 20 years of use in the Houghton study. 2 Q Doctor, what was the metric for exposure 3 in the Gertig and Gates study? 4 MS. CURRY: Objection to form. 5 THE WITNESS: Gertig and Gates looked at 6 frequency of use. Gertig looked at it with a little 7 bit more specificity than Gates did. 8 BY MS. GARBER: 9 Q And what was the metric in the Houghton 10 study? 11 A Duration. 12 MS. CURRY: Object to the form. 13 THE WITNESS: Duration of use. 14 BY MS. GARBER: 15 Q What was the metric in the sister study 16 or the Gonzalez study? 17 MS. CURRY: Object to the form. 18 THE WITNESS: Whether or not the subject 19 had used talc in the preceding 12 months. 20 BY MS. GARBER: 21 Q Didn't you testify in the Echeverria case 22 that without looking at cumulative use, in other 23 words, if you just look at one side of the equation, 24 either frequency or duration, but not frequency 25 times duration, you only see half the story?</p>

<p style="text-align: right;">Page 338</p> <p>1 MS. CURRY: Objection.</p> <p>2 THE WITNESS: I don't believe that that</p> <p>3 is actually what my testimony was.</p> <p>4 MS. CURRY: To form.</p> <p>5 BY MS. GARBER:</p> <p>6 Q Your testimony was that it would be more</p> <p>7 accurate, and it would give a better picture of the</p> <p>8 true risk to see duration times frequency in a</p> <p>9 cohort study.</p> <p>10 Wasn't that your testimony, Doctor?</p> <p>11 MS. CURRY: Objection to form.</p> <p>12 THE WITNESS: Then I don't know that</p> <p>13 you're --</p> <p>14 MS. CURRY: Do you have a copy of the</p> <p>15 testimony?</p> <p>16 THE WITNESS: -- I don't know that you're</p> <p>17 quoting me exactly. I would agree with you that had</p> <p>18 there been information on frequency and duration, it</p> <p>19 would be more informative. But I don't think that</p> <p>20 any of the cohort studies, simply because they</p> <p>21 looked at one metric, i.e., frequency or, i.e.,</p> <p>22 duration, is not informative.</p> <p>23 It would always be nice to have more</p> <p>24 information, but it doesn't discount the fact that</p> <p>25 there is information in these studies which</p>	<p style="text-align: right;">Page 340</p> <p>1 MS. CURRY: Object to the form.</p> <p>2 THE WITNESS: Are we talking about the</p> <p>3 published ones, peer-reviewed, published?</p> <p>4 MS. GARBER: We can start there.</p> <p>5 THE WITNESS: I'm aware of at least</p> <p>6 eight.</p> <p>7 BY MS. GARBER:</p> <p>8 Q There's nine if we count the Taher paper;</p> <p>9 correct?</p> <p>10 A Which has not been published.</p> <p>11 Q Can we agree that each of nine</p> <p>12 meta-analyses, whether published or not, each showed</p> <p>13 a statistically significant increased risk in</p> <p>14 genital talc and risk of ovarian cancer?</p> <p>15 MS. CURRY: Object to the form.</p> <p>16 THE WITNESS: Each of them did report a</p> <p>17 statistically significant odds ratio; yes, but the</p> <p>18 meta-analyses all are different in that some of them</p> <p>19 included the cohort data, but then pulled it out of</p> <p>20 the analysis and this influenced the odds ratio.</p> <p>21 And many of the meta-analyses have simply built upon</p> <p>22 the earlier meta-analyses, so they're reanalyzing</p> <p>23 the same data.</p> <p>24 BY MS. GARBER:</p> <p>25 Q So you think they're just rehashing the</p>
<p style="text-align: right;">Page 339</p> <p>1 demonstrates that there is not an increased risk of</p> <p>2 developing ovarian cancer with perineal application</p> <p>3 of talc.</p> <p>4 BY MS. GARBER:</p> <p>5 Q Amongst the cohorts, the longest</p> <p>6 follow-up was what period of time?</p> <p>7 A Follow-up of the study period itself?</p> <p>8 Q Yes.</p> <p>9 A 24, almost 25 years.</p> <p>10 Q What about the other studies?</p> <p>11 A The follow-up itself, in Houghton, was</p> <p>12 12.4 years. But again, that is -- needs to be</p> <p>13 clarified by the fact that women were asked about</p> <p>14 years of use and there were women in the study that</p> <p>15 already had reported more than 20 years of use.</p> <p>16 Q And what about the Gonzales study, what</p> <p>17 was the period of follow-up in those studies?</p> <p>18 A I believe that was 6.4 years. But I'd</p> <p>19 have to look at the study to know that I have the</p> <p>20 decimal right.</p> <p>21 Q In the meta-analyses that you looked at,</p> <p>22 how many meta-analyses are there with regard to</p> <p>23 talcum powder, genital talcum powder exposure and</p> <p>24 risk of ovarian cancer?</p> <p>25 A Are we talking --</p>	<p style="text-align: right;">Page 341</p> <p>1 same old data, so you discount them?</p> <p>2 MS. CURRY: Object to the form.</p> <p>3 THE WITNESS: I don't discount them. I</p> <p>4 absolutely reviewed them and I considered them in my</p> <p>5 opinion, but I don't think that their findings are</p> <p>6 anything unique or different. I don't think that,</p> <p>7 for example, to hear added anything to the</p> <p>8 information in the field, I think Penninkilampi is</p> <p>9 incomplete.</p> <p>10 I think that the fact that they all</p> <p>11 report similar odds ratio is not at all surprising,</p> <p>12 because they're using the same data.</p> <p>13 BY MS. GARBER:</p> <p>14 Q Do you know what was said about the</p> <p>15 Penninkilampi article by ACOG --</p> <p>16 MS. CURRY: Object to the form.</p> <p>17 MS. GARBER: -- when it was published.</p> <p>18 THE WITNESS: You'll have to show me what</p> <p>19 you're referring to.</p> <p>20 ///</p> <p>21 ///</p> <p>22 ///</p> <p>23 ///</p> <p>24 ///</p> <p>25 ///</p>

<p style="text-align: right;">Page 342</p> <p>1 MS. GARBER: I'm going to mark as 2 Exhibit 34 a document that the title indicates 3 "What's New in Ovarian Cancer, Best Articles From 4 the Past Year." And there are four articles that 5 are included and the Penninkilampi article was 6 listed as number two. 7 (C. Saenz Exhibit 34 was marked for 8 identification.) 9 BY MS. GARBER: 10 Q Did you consider that in your expert 11 opinions with regard to Penninkilampi? 12 A So I've actually read the Penninkilampi 13 article, and I stand by my opinions on this. This 14 is not the opinion of ACOG. This is the opinion of 15 Jason Wright. 16 Q Do you know who Jason Wright is? 17 A I do. 18 Q Do you respect him? 19 MS. CURRY: Object to the form. 20 THE WITNESS: On some issues. I've 21 actually taken issue with some of his other 22 publications in the past. This is not something 23 that is peer reviewed. This is something that he 24 submitted. 25 ///</p>	<p style="text-align: right;">Page 344</p> <p>1 BY MS. GARBER: 2 Q Do you have any opinions about 3 hospital-based versus population-based studies? 4 MS. CURRY: Object to the form. 5 THE WITNESS: With respect to what? 6 BY MS. GARBER: 7 Q Do you think one group is more reliable 8 than another? 9 A So I think -- 10 MS. CURRY: Object to the form. 11 THE WITNESS: -- in general, with respect 12 to epidemiologic analysis, you want to match your 13 subjects as closely as you can to -- you want to 14 match your subjects in your controls, your cases in 15 your controls as closely as you can. 16 So when we're talking about ovarian 17 cancer patients, the hospital-based studies, I 18 think, in these circumstances are going to be a more 19 appropriate match for ovarian cancer patients 20 because they're sick patients. So you're comparing 21 like to like. 22 With the population-based studies in 23 ovarian cancer, I don't really have a -- I don't 24 agree that a general population control person that 25 doesn't have an illness per se such as somebody with</p>
<p style="text-align: right;">Page 343</p> <p>1 BY MS. GARBER: 2 Q The range of odds ratios for the 3 meta-analyses were from 1.22 to 1.4 across those 4 nine studies; correct? 5 A I would have to see exactly, but I will 6 concede with you that I believe you are in the 7 correct range. 8 Q The Health Canada considered the 9 collective meta-analyses in coming to their causal 10 opinion about genital talcum risk of ovarian cancer, 11 didn't they? 12 MS. CURRY: Object to the form. 13 THE WITNESS: They included them in their 14 reference list. 15 BY MS. GARBER: 16 Q IARC considered 2010 -- considered the 17 meta-analyses that were then available at the time 18 of their analysis -- analysis in coming to their 19 opinions regarding genital talc and carcinogenicity. 20 MS. CURRY: Object to the form. 21 THE WITNESS: I don't know that IARC 22 considered the meta-analyses. I think that IARC 23 considered published literature, but I don't 24 actually know that IARC considered the metas. 25 ///</p>	<p style="text-align: right;">Page 345</p> <p>1 ovarian cancer is necessarily an appropriate match 2 control. 3 So I think that's why you see, for 4 example, something like in the Langseth paper, where 5 there's a difference in the studies that find 6 statistically significant odds ratios in the 7 population-based studies versus the hospital-based 8 studies. 9 BY MS. GARBER: 10 Q Doctor, you reviewed the IARC 2012 11 analysis, didn't you? 12 MS. CURRY: Object to the form. 13 THE WITNESS: You mean the monograph? 14 MS. GARBER: Yes, thank you. 15 THE WITNESS: Yes. On asbestos? 16 MS. GARBER: Yes. 17 BY MS. GARBER: 18 Q Did that formulate your opinions about 19 asbestos in this case? 20 A No. 21 MS. CURRY: Object to the form. 22 THE WITNESS: No. 23 MS. SHARKO: So we have about 20 minutes 24 left on the record. 25 MS. GARBER: Let's mark as Exhibit 35.</p>

Page 346

1 Was I supposed to bring a bunch of these? I knew
2 you'd have one.
3 MS. CURRY: According to the CMR, I
4 believe so. I do have my own copy this time.
5 MS. GARBER: All right, I'm glad to see
6 you have your own.
7 (C. Saenz Exhibit 35 was marked for
8 identification.)
9 BY MS. GARBER:
10 Q Doctor, did you read the entirety of this
11 IARC Monograph Volume 100C?
12 A No.
13 Q Which portions did you read?
14 A The portions that pertained to ovarian
15 cancer.
16 Q And the topic of asbestos?
17 A Yes, ma'am.
18 Q You didn't read this IARC Monograph with
19 regard to heavy metals like chromium or nickel, did
20 you?
21 A No, I did not.
22 Q If I could have you turn to page 219.
23 A I'm sorry, say that again.
24 Q Page 219.
25 A Sure.

Page 347

1 Q You've testified in the past, haven't
2 you, that you're not an expert in asbestos; right?
3 A That's correct.
4 Q Under the heading, "Identification of the
5 Agent," the monograph indicates, midway through the
6 paragraph, "The conclusion reached by this monograph
7 about asbestos" --
8 A In this monograph.
9 Q I'll start again. The monograph
10 indicates: "The conclusions reached in this
11 monograph about asbestos and it's carcinogenic risk
12 applied to the six types of fibers, wherever they
13 are found, and that includes talc containing
14 asbestiform fibers."
15 Did I read that correctly?
16 A Yes, ma'am.
17 Q When it indicates the six types of
18 fibers, those are the six type of asbestos fibers
19 listed above; correct?
20 A I believe it's --
21 MS. CURRY: Object to the form.
22 THE WITNESS: I believe it's the six
23 types of fibers that are listed in the title of this
24 section on page 219, yes.
25 ///

Page 348

1 BY MS. GARBER:
2 Q This monograph pertains to asbestos and
3 talc containing asbestiform fibers; right?
4 A That's what it says.
5 Q Are you aware that the IARC Monograph
6 states that the general population can be exposed to
7 asbestos through perineal powder use?
8 MS. CURRY: I'm sorry, where are you
9 reading?
10 THE WITNESS: Where is this in the
11 monograph?
12 MS. GARBER: Turn to 232. Sorry, I was
13 on the wrong page. If you turn to page 232, where
14 it says "Human Exposure."
15 THE WITNESS: Yes.
16 MS. GARBER: Subheading, "Exposure in the
17 General Population." It indicates: "Consumer
18 products, e.g. cosmetics, pharmaceuticals are the
19 primary sources of exposure to talc for the general
20 population. Inhalation and dermal contact, i.e.,
21 through a perineal application of talcum powders are
22 the primary routes of exposure."
23 BY MS. GARBER:
24 Q Did I read that correctly?
25 A Yes.

Page 349

1 Q You read the Heller 1996 paper, correct?
2 MS. CURRY: Object to the form. There
3 are multiple Heller 1996 papers. I'm not sure which
4 one you're referring to.
5 MS. GARBER: Heller 1996 that related to
6 asbestos.
7 THE WITNESS: I don't know. Let me see.
8 I believe that it's on my additional materials
9 reviewed by list, yes. Number 11.
10 BY MS. GARBER:
11 Q Do you --
12 A Oh, I take that back. That's malignant
13 mesotheliomas. Are we talking about the correlation
14 of asbestos fiber burdens and fallopian tubes and
15 ovarian tissue?
16 Q Yes. Did you read that paper?
17 A Yes.
18 Q Do you believe that paper provides
19 support that asbestos can reach the ovarian tissue?
20 MS. CURRY: Object to the form.
21 THE WITNESS: So I don't know how the
22 asbestos that's reported in the Heller paper got
23 there. I don't know if it's inhalation, ingestion.
24 I don't know if it's contamination. I have no way
25 of knowing.

<p style="text-align: right;">Page 350</p> <p>1 BY MS. GARBER:</p> <p>2 Q Okay.</p> <p>3 A And I'm sorry, I think we -- that you</p> <p>4 misquoted. I think that this is Heller 1999. Not</p> <p>5 1996.</p> <p>6 Q On your --</p> <p>7 A Unless I have a typo.</p> <p>8 Q On your reference list, you cite -- you</p> <p>9 cite Heller 1996, asbestos exposure and ovarian</p> <p>10 fiber burden. Did I read that correctly?</p> <p>11 A Oh, I apologize, ma'am. Yes. I was</p> <p>12 looking in the additional materials reviewed, so my</p> <p>13 bad.</p> <p>14 MS. GARBER: I'm going to mark the</p> <p>15 "Heller 1996 Asbestos Exposure and Ovarian Fiber</p> <p>16 Burden" as Exhibit 36.</p> <p>17 (C. Saenz Exhibit 36 was marked for</p> <p>18 identification.)</p> <p>19 BY MS. GARBER:</p> <p>20 Q Doctor, if you could turn to page 438,</p> <p>21 left-hand column.</p> <p>22 Doctor, if you're going to read it, we'll</p> <p>23 go off the record. We're short on time. I didn't</p> <p>24 ask you to read it. I asked you to --</p> <p>25 A I understand that, but I want to --</p>	<p style="text-align: right;">Page 352</p> <p>1 opinions?</p> <p>2 A Right, so I believe that many of those</p> <p>3 citations are the same ones that are reported in the</p> <p>4 IARC Monograph that talks about heavy occupational</p> <p>5 exposure.</p> <p>6 So I did read those and consider those,</p> <p>7 but again, I don't necessarily agree with IARC. I</p> <p>8 think there are problems in this.</p> <p>9 Q Is it your opinion that asbestos is</p> <p>10 associated with ovarian cancer and heavy</p> <p>11 occupational users?</p> <p>12 MS. CURRY: Object to the form.</p> <p>13 THE WITNESS: So I don't necessarily</p> <p>14 agree with IARC's conclusions on that, because I</p> <p>15 think as we've discussed earlier, I believe, that</p> <p>16 there are problems with the five studies that IARC</p> <p>17 looked at, including problems of misclassification,</p> <p>18 problems of using death certificates, and not</p> <p>19 necessarily -- I -- actually identifying whether or</p> <p>20 not these women had peritoneal mesothelioma versus</p> <p>21 ovarian cancer.</p> <p>22 BY MS. GARBER:</p> <p>23 Q Doctor, have you testified that asbestos</p> <p>24 can cause ovarian cancer with heavy occupation</p> <p>25 allege exposure?</p>
<p style="text-align: right;">Page 351</p> <p>1 there's --</p> <p>2 MS. GARBER: Let's go off the record.</p> <p>3 THE WITNESS: -- four Heller papers.</p> <p>4 MS. GARBER: Let's go off the record.</p> <p>5 THE VIDEOGRAPHER: Time is now 6:05.</p> <p>6 Going off the record.</p> <p>7 (Break in the deposition taken at 6:06 p.m.)</p> <p>8 0o0</p> <p>9 (The deposition resumed at 6:07 p.m.)</p> <p>10 0o0</p> <p>11 THE VIDEOGRAPHER: Time is now 6:06.</p> <p>12 Back on the record.</p> <p>13 BY MS. GARBER:</p> <p>14 Q At page 438, left-hand column. Beginning</p> <p>15 in the first paragraph, where it begins, "Asbestos,"</p> <p>16 it indicates, "Asbestos causes" --</p> <p>17 A 438, beginning in the left-hand column.</p> <p>18 First paragraph or second paragraph?</p> <p>19 Q I said the first paragraph.</p> <p>20 A First paragraph. Okay. I'm right there</p> <p>21 with you.</p> <p>22 Q "Asbestos causes malignant mesothelioma</p> <p>23 and there is evidence to support it as an etiology</p> <p>24 in ovarian carcinoma as well." And some citations.</p> <p>25 Did you consider that in formulating your</p>	<p style="text-align: right;">Page 353</p> <p>1 MS. CURRY: Object to the form.</p> <p>2 THE WITNESS: I'd have to look at my</p> <p>3 testimony to know if that's exactly what I said.</p> <p>4 BY MS. GARBER:</p> <p>5 Q Well, if it's the truth, wouldn't you</p> <p>6 remember it, Doctor?</p> <p>7 MS. CURRY: Object to the form.</p> <p>8 BY MS. GARBER:</p> <p>9 Q Do you have to see your old testimony to</p> <p>10 see what your opinions are?</p> <p>11 MS. CURRY: Object to the form.</p> <p>12 THE WITNESS: Ma'am, I gave you my</p> <p>13 opinion today. I don't know that you're reading</p> <p>14 accurately from what that transcript is and that</p> <p>15 transcript was from, I believe, if that's the trial</p> <p>16 transcript, July of 2017. If it was the deposition,</p> <p>17 it's almost three years ago now so -- or two years</p> <p>18 ago. So I would need to see it to know --</p> <p>19 BY MS. GARBER:</p> <p>20 Q Has your opinion changed?</p> <p>21 A I don't know that you're reading my</p> <p>22 testimony accurately. And I would ask to be able to</p> <p>23 see my testimony to see if that's actually true. I</p> <p>24 gave you my opinion today. I'm simply asking to see</p> <p>25 if I can look at what you're reading to see if</p>

<p style="text-align: right;">Page 354</p> <p>1 you're reading it accurately.</p> <p>2 Q It was formerly your opinion prior to the</p> <p>3 MDL report and today's testimony that asbestos could</p> <p>4 cause ovarian cancer in heavy occupational use, was</p> <p>5 it not?</p> <p>6 MS. CURRY: Object to the form.</p> <p>7 THE WITNESS: Ma'am, I'm not going to</p> <p>8 comment on that unless you actually let me see the</p> <p>9 testimony and see what I said.</p> <p>10 MS. GARBER: I will read it to you first.</p> <p>11 THE WITNESS: Ma'am, that's not going to</p> <p>12 be good enough.</p> <p>13 BY MS. GARBER:</p> <p>14 Q "But my question is simple."</p> <p>15 I'm going to read it, and then I'll show</p> <p>16 it to you.</p> <p>17 "But my question simple. Answer it,</p> <p>18 please. So we'll know which side of the</p> <p>19 equation you're on. Does asbestos cause</p> <p>20 ovarian cancer, Dr. Saenz?"</p> <p>21 Your answer is: "Answer: Yes, with</p> <p>22 heavy occupational exposure. Yes, if</p> <p>23 exposed enough, that's what I said."</p> <p>24 "Well, ma'am, you're not an asbestos</p> <p>25 specialist, are you?"</p>	<p style="text-align: right;">Page 356</p> <p>1 trial, Doctor --</p> <p>2 A Ma'am, I'm not done.</p> <p>3 Q Okay.</p> <p>4 A In the context of being asked about what</p> <p>5 I thought about IARC's report and whether or not</p> <p>6 IARC showed that in the context, did IARC report</p> <p>7 that asbestos causes ovarian cancer with heavy</p> <p>8 occupational exposure. I recorded that. But it was</p> <p>9 with the qualifications that I had problems with the</p> <p>10 studies in the IARC Monograph.</p> <p>11 Q I understand that.</p> <p>12 A That's exactly what I've said here today.</p> <p>13 Q Is your --</p> <p>14 A I have not changed my opinion.</p> <p>15 Q I understand that. Is your opinion --</p> <p>16 no, I don't understand that. Is your opinion today</p> <p>17 that asbestos causes ovarian cancer?</p> <p>18 MS. CURRY: Object to the form.</p> <p>19 THE WITNESS: My opinion today is that I</p> <p>20 don't think the IARC Monograph conclusions are</p> <p>21 correct. I believe that there are problems with</p> <p>22 those studies. And my opinion, as I stated then in</p> <p>23 the Ingham trial, is that there are problems with</p> <p>24 those studies.</p> <p>25 And so IARC makes that conclusion,</p>
<p style="text-align: right;">Page 355</p> <p>1 "No, I am not."</p> <p>2 MS. CURRY: What transcript are you</p> <p>3 reading from?</p> <p>4 MS. GARBER: I'm reading from the Ingham</p> <p>5 testimony at trial.</p> <p>6 MS. CURRY: If you need to see additional</p> <p>7 pages, please let Counsel know.</p> <p>8 BY MS. GARBER:</p> <p>9 Q Is that your testimony? Did I read it</p> <p>10 correctly?</p> <p>11 A No, ma'am, you're not reading this</p> <p>12 accurately, because earlier in this transcript, I'm</p> <p>13 asked about what I think of the IARC monograph. And</p> <p>14 that's actually very consistent with what I'm saying</p> <p>15 here today.</p> <p>16 In this transcript, I said, I read the</p> <p>17 IARC Monograph. I've read the studies in the</p> <p>18 monograph and I know the conclusion that IARC came</p> <p>19 to. And I think there are some problems with the</p> <p>20 studies that they used to come to that conclusion,</p> <p>21 but that is their conclusion. I understand that,</p> <p>22 but that was limited to heavy occupational exposure.</p> <p>23 So in the context --</p> <p>24 BY MS. GARBER:</p> <p>25 Q But you've said -- you've said in the</p>	<p style="text-align: right;">Page 357</p> <p>1 but I don't necessarily agree with that conclusion.</p> <p>2 BY MS. GARBER:</p> <p>3 Q But Dr. Saenz, the record speaks for</p> <p>4 itself.</p> <p>5 A Ma'am, you can't cherry-pick one line.</p> <p>6 The context of which --</p> <p>7 Q No, now you're interrupting me. I'm</p> <p>8 trying to ask you a question, I'm short on time and</p> <p>9 you know it. The IARC -- you testified in the</p> <p>10 Ingham trial, and you admitted to Mr. Lenear, that</p> <p>11 heavy occupational use of asbestos was associated</p> <p>12 with ovarian cancer.</p> <p>13 Now you're here today saying something</p> <p>14 differently, that it doesn't, correct?</p> <p>15 MS. CURRY: Object to the form, misstates</p> <p>16 the testimony.</p> <p>17 THE WITNESS: I'm not saying anything any</p> <p>18 different than I said in my testimony --</p> <p>19 MS. GARBER: I just need to know what</p> <p>20 your opinion is --</p> <p>21 MS. SHARKO: Don't interrupt the witness,</p> <p>22 come on.</p> <p>23 BY MS. GARBER:</p> <p>24 Q When you show up at any hearing or trial,</p> <p>25 are you going to tell the court and jury that</p>

<p style="text-align: right;">Page 358</p> <p>1 asbestos does or doesn't cause ovarian cancer?</p> <p>2 That's all I need to know, and we're pretty much</p> <p>3 done.</p> <p>4 MS. CURRY: Object to the form.</p> <p>5 THE WITNESS: My testimony today is</p> <p>6 consistent with what I said in testimony at trial at</p> <p>7 the Ingham trial. I take issue with the conclusions</p> <p>8 that IARC has drawn. But the conclusions that IARC</p> <p>9 has drawn is that ovarian cancer can be caused by</p> <p>10 asbestos, but it's limited to heavy occupational</p> <p>11 exposure. I don't agree with those conclusions.</p> <p>12 BY MS. GARBER:</p> <p>13 Q You have stated at trial, haven't you,</p> <p>14 asbestos can cause inflammation at the cellular</p> <p>15 level?</p> <p>16 MS. CURRY: Object to the form. May we</p> <p>17 see the testimony?</p> <p>18 THE WITNESS: I don't know that I said</p> <p>19 that.</p> <p>20 BY MS. GARBER:</p> <p>21 Q Have you said asbestos generates R-O-S</p> <p>22 and N-O-S?</p> <p>23 MS. CURRY: Object to the form.</p> <p>24 BY MS. GARBER:</p> <p>25 Q Have you testified to that?</p>	<p style="text-align: right;">Page 360</p> <p>1 THE WITNESS: Again, ma'am, I'd like to</p> <p>2 see the testimony to know the exact context in which</p> <p>3 you're pulling that from.</p> <p>4 MS. SHARKO: Aren't we now at seven</p> <p>5 hours?</p> <p>6 MS. GARBER: You've testified that</p> <p>7 asbestos can cause resistance to apoptosis, which is</p> <p>8 an established mechanistic event for the development</p> <p>9 of ovarian cancer, haven't you?</p> <p>10 MS. CURRY: Object to the form.</p> <p>11 THE WITNESS: You would have to show me</p> <p>12 that testimony, ma'am.</p> <p>13 BY MS. GARBER:</p> <p>14 Q Do you ever tell your patients that</p> <p>15 asbestos is a risk factor for ovarian cancer?</p> <p>16 A No, I do not.</p> <p>17 Q Are you -- if a patient asks you, Doctor,</p> <p>18 is there asbestos in the Johnson & Johnson products</p> <p>19 that I'm using on my genitals, how would you reply?</p> <p>20 A I would reply to them that I do not know</p> <p>21 what the actual makeup of the baby powder products</p> <p>22 are, but that the literature that I have reviewed as</p> <p>23 a paid expert for Johnson & Johnson does not show</p> <p>24 any consistency that using baby powder products in</p> <p>25 the perineal region increases the risk of developing</p>
<p style="text-align: right;">Page 359</p> <p>1 MS. CURRY: Object to the form. Can we</p> <p>2 see the testimony?</p> <p>3 THE WITNESS: I can't recall saying that</p> <p>4 specifically. I would be happy to review it for</p> <p>5 you.</p> <p>6 BY MS. GARBER:</p> <p>7 Q Have you testified that asbestos is</p> <p>8 genotoxic?</p> <p>9 MS. CURRY: Object to the form.</p> <p>10 THE WITNESS: I cannot verify for you</p> <p>11 that I have testified to that. I'd be happy to</p> <p>12 review the testimony for you.</p> <p>13 BY MS. GARBER:</p> <p>14 Q Have you testified that asbestos can</p> <p>15 cause epigenetic alterations?</p> <p>16 MS. CURRY: Object to the form.</p> <p>17 THE WITNESS: I don't know that I have</p> <p>18 said that phrase exactly, ma'am. I'd be happy to</p> <p>19 look at the testimony.</p> <p>20 BY MS. GARBER:</p> <p>21 Q Asbestos can alter signaling pathways</p> <p>22 which is an established mechanistic event for some</p> <p>23 cancers, including ovarian cancer. You agreed to</p> <p>24 that, didn't you?</p> <p>25 MS. CURRY: Object to the form.</p>	<p style="text-align: right;">Page 361</p> <p>1 ovarian cancer.</p> <p>2 Q And I want you -- I'm going to ask you a</p> <p>3 final hypothetical. I want you to assume that there</p> <p>4 is asbestos in Johnson & Johnson baby powder</p> <p>5 products or Johnson & Johnson talcum powder</p> <p>6 products. And if a patient asked you, Doctor, is it</p> <p>7 safe for me to use that product on my genitals, what</p> <p>8 would be your reply?</p> <p>9 MS. CURRY: Object to the form.</p> <p>10 THE WITNESS: My reply would be, to my</p> <p>11 patient, ma'am, I've done a thorough review of the</p> <p>12 literature, the case control studies, the biologic</p> <p>13 plausibility, the cohort studies, it is my review</p> <p>14 and my opinion that there is no increased risk of</p> <p>15 you developing ovarian cancer from the use of</p> <p>16 Johnson & Johnson baby powder products and I would</p> <p>17 disclose that I am a paid expert in this litigation</p> <p>18 testimony.</p> <p>19 BY MS. GARBER:</p> <p>20 Q You would counsel your patient to put a</p> <p>21 product that has asbestos in it on her genitals?</p> <p>22 MS. CURRY: Object to the form, misstates</p> <p>23 the testimony.</p> <p>24 THE WITNESS: I don't believe that there</p> <p>25 is any -- any increased risk of developing ovarian</p>

Cheryl Saenz, M.D.

<p style="text-align: right;">Page 362</p> <p>1 cancer with the use of Johnson & Johnson baby powder</p> <p>2 products. And if asbestos is in the baby powder and</p> <p>3 the baby powder is the vehicle by which the asbestos</p> <p>4 is being delivered there, then the baby powder</p> <p>5 literature should show an increased risk of</p> <p>6 developing ovarian cancer. And it does not.</p> <p>7 BY MS. GARBER:</p> <p>8 Q Doctor, based on the IARC assessment of</p> <p>9 asbestos and risk of ovarian cancer, and I want you</p> <p>10 now to assume that there is asbestos in Johnson &</p> <p>11 Johnson talcum powder products. It is your</p> <p>12 testimony that you would counsel your patient that</p> <p>13 it is safe, based on your review of the literature,</p> <p>14 to put that product containing asbestos on her</p> <p>15 genitals, that's your testimony?</p> <p>16 MS. CURRY: Object to the form.</p> <p>17 THE WITNESS: Yes.</p> <p>18 MS. GARBER: Okay. Thank you. I'm</p> <p>19 finished for now.</p> <p>20 THE VIDEOGRAPHER: The time is now 6:17.</p> <p>21 Going off the record.</p> <p>22 (Break in the deposition taken at 6:18 p.m.)</p> <p>23 0o0</p> <p>24 (The deposition resumed at 6:18 p.m.)</p> <p>25 0o0</p>	<p style="text-align: right;">Page 364</p> <p>1 I, CHERYL SAENZ, M.D., do hereby declare</p> <p>2 under penalty of perjury that I have read the</p> <p>3 foregoing transcript; that I have made any</p> <p>4 corrections as noted in ink, initialed by me; that</p> <p>5 my testimony as contained herein, as corrected, is</p> <p>6 true and correct.</p> <p>7</p> <p>8 EXECUTED this _____ day of</p> <p>9 _____, 20____, at _____,</p> <p>10 (City)</p> <p>11 _____.</p> <p>12 (State)</p> <p>13</p> <p>14 _____</p> <p>15 CHERYL SAENZ, M.D.</p> <p>16</p> <p>17</p> <p>18</p> <p>19</p> <p>20</p> <p>21</p> <p>22</p> <p>23</p> <p>24</p> <p>25</p>
<p style="text-align: right;">Page 363</p> <p>1 THE VIDEOGRAPHER: The time is now 6:17.</p> <p>2 Back on the record.</p> <p>3 EXAMINATION</p> <p>4 -o0o-</p> <p>5 BY MS. CURRY:</p> <p>6 Q Dr. Saenz, I just have one final question</p> <p>7 for you, and that is, having heard and seen</p> <p>8 everything presented to you today by plaintiffs'</p> <p>9 counsel, do you stand by all of your opinions in</p> <p>10 your expert report in this case?</p> <p>11 A I stand by everything that is in my</p> <p>12 expert report. I stand by everything that I have</p> <p>13 expressed as an opinion today.</p> <p>14 MS. CURRY: Thank you. No further</p> <p>15 questions.</p> <p>16 MS. GARBER: No further questions.</p> <p>17 THE VIDEOGRAPHER: The time is now 6:18.</p> <p>18 This concludes the deposition. Going off the</p> <p>19 record.</p> <p>20 (The deposition was concluded at 6:19 p.m.)</p> <p>21 0o0</p> <p>22</p> <p>23</p> <p>24</p> <p>25</p>	<p style="text-align: right;">Page 365</p> <p>1 REPORTER'S CERTIFICATE</p> <p>2 I, Valerie C. Rodriguez, a Certified</p> <p>3 Shorthand Reporter for the State of California, do</p> <p>4 hereby certify:</p> <p>5 That prior to being examined, CHERYL</p> <p>6 SAENZ, M.D., the witness named in the foregoing</p> <p>7 deposition, was by me duly sworn;</p> <p>8 That said deposition was taken before me</p> <p>9 at the time and place set forth herein and was</p> <p>10 stenographically reported by me in shorthand and</p> <p>11 thereafter transcribed into typewriting using</p> <p>12 computer-aided transcription, and I hereby certify</p> <p>13 that said deposition is a full, true, and correct</p> <p>14 transcript; that the dismantling, unsealing, or</p> <p>15 unbinding of the original transcript will render the</p> <p>16 reporter's certificate null and void.</p> <p>17 I further certify that I am neither</p> <p>18 counsel for, nor related to any party to said</p> <p>19 action, nor in any way interested in the outcome</p> <p>20 thereof. IN WITNESS WHEREOF, I have subscribed my</p> <p>21 name this 15th day of March, 2019.</p> <p>22</p> <p>23</p> <p>24 _____</p> <p>25 VALERIE C. RODRIGUEZ</p> <p>CSR No. 12871 (orig. 6980)</p>

Cheryl Saenz, M.D.

Page 366

1 DEPOSITION ERRATA SHEET

2 Case Name: IN RE JOHNSON & JOHNSON

3 Name of Witness: CHERYL SAENZ, M.D.

4 Date of Deposition: MARCH 13, 2019, 2019

5 Job No.: 210344

6 Reason Codes: 1. To clarify the record.

7 2. To conform to the facts.

8 3. To correct transcription errors.

9

Page _____ Line _____ Reason _____

10

From _____ to

11

Page _____ Line _____ Reason _____

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From _____ to

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Page _____ Line _____ Reason _____

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From _____ to

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Page _____ Line _____ Reason _____

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From _____ to

18

19

Page _____ Line _____ Reason _____

20

21 _____ Subject to the above changes, I certify
that the transcript is true and correct.

22

23 _____ No changes have been made. I certify that
the transcript is true and correct.

24

25

_____ CHERYL SAENZ, M.D.

Exhibit 10

1 IN THE UNITED STATES DISTRICT COURT
2 FOR THE EASTERN DISTRICT OF NEW JERSEY
3 - - -
4

5 IN RE: JOHNSON & :
6 JOHNSON TALCUM POWDER :
7 PRODUCTS MARKETING, :
8 SALES PRACTICES, AND : NO. 16-2738
9 PRODUCTS LIABILITY : (FW) (LHG)
10 LITIGATION :
11 :
12 THIS DOCUMENT RELATES :
13 TO ALL CASES :

14 - - -
15 March 19, 2019
16 - - -
17

18 Videotaped deposition of
19 BENJAMIN G. NEEL, M.D., Ph.D., taken
20 pursuant to notice, was held at Skadden
21 Arps, Four Times Square, New York, New
22 York, beginning at 8:56 a.m., on the
23 above date, before Michelle L. Gray, a
24 Registered Professional Reporter,
25 Certified Shorthand Reporter, Certified
26 Realtime Reporter, and Notary Public.

27 - - -
28 GOLKOW LITIGATION SERVICES
29 877.370.3377 ph| 917.591.5672
30 deps@golkow.com
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32
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1 - - -
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3 - - -

5 Testimony of:

6 BENJAMIN G. NEEL, M.D., Ph.D.
7 By Dr. Thompson 12

10 - - -
11 E X H I B I T S
12 - - -

13 NO.	13 DESCRIPTION	13 PAGE
14 Neel-1	14 Notice of Deposition	16
15 Neel-2	15 Expert Report	18
16	16 Of Benjamin G. Need	
17	17 MD, Ph.D.	
18	18 2/25/19	
19 Neel-3	19 Materials	19
20 Neel-4	20 Considered List	
21	21 Appendix A	53
22	22 GWAS Associations	
23	23 For Ovarian Carcinomas	
24	24 Curriculum Vitae	57
	2/22/19	

NO.	DESCRIPTION	PAGE
Neel-23	Does Long-Term Talc Exposure Have a Carcinogenic Effect (Keskin)	257
Neel-24	Effects of Talc On the Rat Ovary (Hamilton)	260
Neel-25	Federal Register 12/19/16 Volume 81 No. 243	261
Neel-26	The Relationship Between Perineal Cosmetic Talc (Heller)	266
Neel-27	Ovarian Cancers Evolving Paradigms In Research & Care The National Academies Of Sciences Engineering Medicine	288
Neel-28	Smooth Reference Equations for Slow Vital Capacity And Flow Volume Curve Indexes Correspondence	304
Neel-29	Curriculum Vitae Of Dr. Saed	312

	- - -	
	E X H I B I T S (Cont'd.)	
	- - -	
5	NO.	PAGE
6	Neel-30	379
7	Pycnogenol Reduces Talc-Induced Neoplastic Transformation (Buz'Zard)	
8		
9	Neel-31	390
10	Alterations in Gene Expression in Human Mesothelial Cells (Shukla)	
11		
12	Neel-32	399
13	The Primary Role Or Iron-Mediated Lipid Peroxidation (Akhtar)	
14		
15	Neel-33	416
16	Cytotoxicity and Apoptosis Induction By Nanoscale Talc Particles (Akhtar)	
17		
18		
19		
20		
21		
22		
23		
24		

<p style="text-align: right;">Page 10</p> <p>1 - - -</p> <p>2 DEPOSITION SUPPORT INDEX</p> <p>3 - - -</p> <p>4</p> <p>5 Direction to Witness Not to Answer</p> <p>6 PAGE LINE</p> <p>7 None.</p> <p>8 Request for Production of Documents</p> <p>9 PAGE LINE</p> <p>10 None.</p> <p>11 Stipulations</p> <p>12 PAGE LINE</p> <p>13 None.</p> <p>14 Questions Marked</p> <p>15 PAGE LINE</p> <p>16 None.</p> <p>17</p> <p>18</p> <p>19</p> <p>20</p> <p>21</p> <p>22</p> <p>23</p> <p>24</p>	<p style="text-align: right;">Page 12</p> <p>1 EXAMINATION</p> <p>2 - - -</p> <p>3 BY DR. THOMPSON:</p> <p>4 Q. Good morning, Dr. Neel.</p> <p>5 A. Good morning.</p> <p>6 Q. My name is Margaret</p> <p>7 Thompson, and I'll be taking your</p> <p>8 deposition today. Have you ever had your</p> <p>9 deposition taken before?</p> <p>10 A. Yes.</p> <p>11 Q. What were the circumstances?</p> <p>12 A. In a -- in a case, the</p> <p>13 so-called Potti-Nevins case. I gave a</p> <p>14 deposition for -- in the -- for the</p> <p>15 defendant. It was a matter involving</p> <p>16 scientific fraud at Duke University.</p> <p>17 Q. Oh. That's my alma mater.</p> <p>18 A. And I also was deposed in a</p> <p>19 malpractice suit when I was a resident in</p> <p>20 Boston.</p> <p>21 Q. As a defendant?</p> <p>22 A. As a defendant.</p> <p>23 Q. And are those the only two</p> <p>24 times --</p>
<p style="text-align: right;">Page 11</p> <p>1 - - -</p> <p>2 THE VIDEOGRAPHER: We are</p> <p>3 now on the record. My name is</p> <p>4 Henry Marte. I'm a videographer</p> <p>5 with Golkow Litigation Services.</p> <p>6 Today's date is March 19,</p> <p>7 2019, and the time is 8:56 a.m.</p> <p>8 This videotaped deposition</p> <p>9 is being held at Four Times</p> <p>10 Square, New York, New York, in the</p> <p>11 matter of Talcum Powder</p> <p>12 Litigation.</p> <p>13 The deponent today is Dr.</p> <p>14 Benjamin Neel.</p> <p>15 All appearances are noted on</p> <p>16 the stenographic record.</p> <p>17 Will the court reporter</p> <p>18 please administer the oath to the</p> <p>19 witness.</p> <p>20 - - -</p> <p>21 ... BENJAMIN G. NEEL, M.D., Ph.D.,</p> <p>22 having been first duly sworn, was</p> <p>23 examined and testified as follows:</p> <p>24 - - -</p>	<p style="text-align: right;">Page 13</p> <p>1 A. Yes.</p> <p>2 Q. -- that you've had your</p> <p>3 deposition taken?</p> <p>4 And I assume the scientific</p> <p>5 fraud case was at least over four years</p> <p>6 ago, right?</p> <p>7 A. It was a little over four</p> <p>8 years ago, right before the -- the</p> <p>9 deposition was taken right before I</p> <p>10 started at NYU Langone, which was</p> <p>11 January 2015. So the deposition was</p> <p>12 taken in October of 2014, so Columbus Day</p> <p>13 weekend.</p> <p>14 Q. Okay. And you're aware that</p> <p>15 the purpose of today is for me to gain a</p> <p>16 thorough understanding of your opinions</p> <p>17 and the basis for those opinions?</p> <p>18 A. Yes.</p> <p>19 Q. Your report states that your</p> <p>20 opinions are given to a reasonable degree</p> <p>21 of scientific certainty.</p> <p>22 What does that mean to you?</p> <p>23 A. It means that I've</p> <p>24 considered all of the papers and also</p>

Page 14

1 additional information that is contained
 2 in my report. And based on my more than
 3 30 years of scientific credentials and
 4 experience in the cancer biology and
 5 cellular molecular biology field, that I
 6 have offered my opinion based on that
 7 criteria, those criteria.
 8 Q. And how confident do you
 9 have to be in your opinions to be able to
 10 claim that it's a reasonable degree?
 11 A. I'm quite confident in my
 12 opinions on this matter based on my
 13 30 years of experience.
 14 Q. Would that be 100 percent?
 15 A. I'm 100 percent -- I
 16 wouldn't write it if I wasn't 100 percent
 17 confident in my opinions.
 18 Q. And Dr. Neel, you are a
 19 medical doctor as well as a Ph.D.
 20 researcher, correct?
 21 A. That's correct.
 22 Q. Do you currently see
 23 patients?
 24 A. No.

Page 15

1 Q. When did you last have a
 2 clinical practice?
 3 A. 19 -- well I never had a
 4 private practice or an individual
 5 practice. I stopped seeing patients when
 6 I began my faculty position at Harvard
 7 Medical School in 1988.
 8 Q. After residency?
 9 A. Yes.
 10 Q. In internal medicine?
 11 A. Yes.
 12 Q. And do you currently
 13 diagnose ovarian cancer in women?
 14 A. No.
 15 Q. Do you treat women with
 16 ovarian cancer?
 17 A. No.
 18 Q. Have you ever treated women
 19 with ovarian cancer?
 20 A. Only in the context of my
 21 health staff training.
 22 Q. Okay. And would that be the
 23 last time that you performed a pelvic
 24 exam --

Page 16

1 A. Yes.
 2 Q. -- as well?
 3 So let me just review some
 4 of the ground rules today to remind you.
 5 If you don't understand a question,
 6 please let me know so I can hopefully put
 7 it in a form where you do understand.
 8 Okay?
 9 A. Okay.
 10 Q. And I'll do my best to let
 11 you finish your answer, and probably best
 12 for you to let me finish my question too,
 13 for lots of reasons, but primarily so our
 14 court reporter can get both of our
 15 statements down without any problems.
 16 Okay?
 17 A. Sure.
 18 Q. And if you need a break,
 19 just let me know --
 20 A. Okay.
 21 Q. -- and we'll take one.
 22 I've marked Exhibit 1 as a
 23 notice of deposition.
 24 (Document marked for

Page 17

1 identification as Exhibit
 2 Neel-1.)
 3 BY DR. THOMPSON:
 4 Q. Have you seen this document,
 5 Dr. Neel?
 6 A. Yes.
 7 Q. When did you see it?
 8 A. Yesterday.
 9 Q. And I understand that
 10 objections have been filed. But -- and
 11 did you bring anything with you today in
 12 response to this notice of deposition?
 13 A. No.
 14 Q. For example, Number 3 says a
 15 copy of your complete file or files. Do
 16 you have a file related to the talcum
 17 powder litigation?
 18 A. Only insofar as I collect
 19 the papers for my report, yes.
 20 Q. How do you collect those?
 21 A. On my computer.
 22 Q. Do you have a certain
 23 location where you maintain those files?
 24 A. Yes.

<p style="text-align: right;">Page 18</p> <p>1 Q. And do you have any notes or 2 highlights on the articles? 3 A. On the articles, no. 4 Q. Any notes or -- in the file 5 where you keep your articles? 6 A. Only insofar as I, you know, 7 was preparing my report. There's some 8 notes about the text that I'm going to 9 use in my report. 10 Q. Okay. I also have marked a 11 copy of your expert report. 12 (Document marked for 13 identification as Exhibit 14 Neel-2.) 15 BY DR. THOMPSON: 16 Q. Is this the report that you 17 were referring to that -- 18 A. Yes. 19 Q. -- you kept drafts on your 20 computer? 21 A. Yes. 22 MS. SHARKO: For the record, 23 this is Exhibit 2? 24 DR. THOMPSON: This is</p>	<p style="text-align: right;">Page 20</p> <p>1 the references that are cited by -- in 2 numerical order in the report. 3 Q. And I'm also marking 4 Exhibit 3, which is an -- additional 5 references that -- it's titled "Materials 6 Considered." 7 And what is the list of 8 materials considered? 9 A. I'm a little confused by 10 your question. It says what they are. 11 Q. How does that differ from 12 the references that are attached to your 13 expert report? 14 A. Oh well, if I cited 15 something directly in the report, it's in 16 the references. If there were things 17 that I was given or that I looked 18 through, that's on materials considered. 19 Q. Were you -- were you given 20 the references on the materials 21 considered by counsel? 22 A. A subset of the materials 23 were sent to me at the beginning. I made 24 several other searches of my own and</p>
<p style="text-align: right;">Page 19</p> <p>1 Exhibit 2. 2 MS. SHARKO: Shall we be 3 calling these Neel-1 and 2? 4 MS. O'DELL: I think 5 Michelle will write that in 6 afterwards. 7 BY DR. THOMPSON: 8 Q. And we'll come back, of 9 course, to that report throughout the 10 day. So feel free to keep that close by 11 if you'd like to. 12 (Document marked for 13 identification as Exhibit 14 Neel-3.) 15 BY DR. THOMPSON: 16 Q. And I've marked as Exhibit 3 17 the -- and you say that attached to your 18 report are the references that you 19 listed. And are those references that 20 are actually cited or referred to in the 21 report itself? 22 A. Can I -- may I look? 23 Q. Yes, please. 24 A. Yes. These references are</p>	<p style="text-align: right;">Page 21</p> <p>1 downloaded those papers. And some of the 2 papers I was unable to easily access from 3 my remote location. And I asked the 4 lawyers to have them sent to me. So some 5 of them I got that way. 6 Q. Would you be able to 7 identify which you found yourself and 8 which you were provided to by the 9 lawyers? 10 A. Not easily. I mean, I went 11 through and I spent many hours doing 12 this. So I'm not sure. Over time, that 13 blurs a little. 14 Q. And I assume that the expert 15 reports and deposition transcripts were 16 provided to you, correct? 17 A. Yes. 18 Q. When was -- when were you 19 first contacted by lawyers representing 20 Johnson & Johnson about serving as an 21 expert? 22 A. In May of 2017 I believe. 23 Q. And who contacted you? 24 A. John Winter.</p>

<p style="text-align: right;">Page 22</p> <p>1 Q. And what did Mr. Winter ask 2 you to do?</p> <p>3 A. He asked me if I would be 4 interested in considering being an expert 5 witness in the talc litigation.</p> <p>6 Q. And what did you agree to do 7 at that time?</p> <p>8 A. I agreed to look at the 9 materials that he gave me and make a 10 decision subsequently.</p> <p>11 Q. Were you asked at that time 12 to offer any criticisms of any 13 plaintiffs' experts?</p> <p>14 MS. SHARKO: Well, I'm 15 going -- I'm going to object at 16 this point. Isn't this privileged 17 conversations between counsel and 18 the witness?</p> <p>19 DR. THOMPSON: I believe 20 what he was asked to do at the 21 initiation is fair.</p> <p>22 MS. SHARKO: I think that's 23 privileged conversations between 24 the lawyer and the witness.</p>	<p style="text-align: right;">Page 24</p> <p>1 misunderstood.</p> <p>2 Did he -- was any of that 3 material that he asked you to look at, 4 did that include defense -- plaintiff 5 expert reports?</p> <p>6 A. At the -- the initial batch 7 of materials that I -- that I got had no 8 expert reports from anyone in it.</p> <p>9 Q. Okay. Were you asked to do 10 any experiments?</p> <p>11 A. No.</p> <p>12 Q. Did you offer to do any 13 experiments?</p> <p>14 A. No. I wouldn't be allowed.</p> <p>15 Q. Why is that?</p> <p>16 A. Because it would be a 17 conflict of interest violation of my 18 institution.</p> <p>19 Q. What is your institution's 20 conflict of interest policy?</p> <p>21 A. Well, I mean, that's a 22 pretty broad question. Do you want to 23 maybe -- I mean, my conflict -- we have a 24 very long policy which I have not</p>
<p style="text-align: right;">Page 23</p> <p>1 DR. THOMPSON: Okay. All 2 right.</p> <p>3 MS. SHARKO: You can ask -- 4 you can ask him what he did. I 5 don't think you can ask him about 6 discussions between the lawyer and 7 the witness.</p> <p>8 BY DR. THOMPSON:</p> <p>9 Q. In that initial evaluation 10 that you performed to look, did that 11 include evaluating any expert reports 12 from plaintiffs?</p> <p>13 A. The initial -- are you 14 talking about the initial meeting with 15 Mr. Winter?</p> <p>16 Q. Well, you -- you said that 17 Mr. Winter furnished you with some 18 literature to review, correct?</p> <p>19 A. No. I think I said -- maybe 20 I misspoke. But I believe I said that 21 Mr. Winter asked me if I would be willing 22 to look at some material, and I said yes 23 at our initial meeting.</p> <p>24 Q. Okay. I may have</p>	<p style="text-align: right;">Page 25</p> <p>1 committed to memory.</p> <p>2 Q. Okay. Did -- have you 3 disclosed to your institution that you're 4 serving as an expert for Johnson & 5 Johnson?</p> <p>6 A. Yes.</p> <p>7 Q. And what details did you 8 have to provide regarding that?</p> <p>9 A. Just the name of the law 10 firm that I was working with. I don't 11 remember the name of Mr. Winter's law 12 firm. Because I recently revised the 13 disclosure because I'm working mostly 14 with Ms. Sharko now which is a different 15 firm.</p> <p>16 Q. And why would your 17 institution prevent you from doing any 18 experiments?</p> <p>19 A. I -- I can't comment on 20 the --</p> <p>21 MS. SHARKO: Object to the 22 form.</p> <p>23 THE WITNESS: I can't 24 comment on the basis of the</p>

<p style="text-align: right;">Page 26</p> <p>1 conflict of interest policy. I 2 can only tell you what it is. 3 BY DR. THOMPSON: 4 Q. And what aspect or what 5 language in that policy has led you to 6 believe that you would be unable to do 7 any experiments? 8 A. Because, for any kind of -- 9 we're not allowed to take financial 10 remuneration from anyone and at the same 11 time do laboratory experiments on the 12 topic. That's considered a conflict of 13 interest as I understand the conflict of 14 interest policy. 15 Q. So what -- what entities 16 would that include? 17 MS. SHARKO: Object to the 18 form. 19 BY DR. THOMPSON: 20 Q. Pharmaceutical companies? 21 A. Yes. If I -- if I get 22 funding -- if I get compensation, private 23 compensation from a pharmaceutical 24 company, or if I own equity in a</p>	<p style="text-align: right;">Page 28</p> <p>1 or any compensation from the company. It 2 was not -- it was just laboratory 3 funding. 4 When I was at Harvard 5 Medical School, I believe in the third -- 6 no, it would have been more like the 7 fourth or fifth year that I was a faculty 8 member, I had a grant from Roche 9 Pharmaceuticals. That was a two-year 10 grant, and it was a competitive grant 11 where Harvard had a -- Harvard, I think 12 it was the department of biochemistry -- 13 one of the departments that I was 14 affiliated with at Harvard, had a -- a 15 relationship with Roche where you could 16 submit competitive grants and then they 17 were reviewed by a group that included 18 Harvard faculty and Roche faculty. And 19 they chose the ones they were interested 20 in. And then so I believe it was a 21 \$75,000 grant that I got for two years. 22 Q. Okay. And -- 23 A. And that was on SHIP1, which 24 I'm also an expert in. I identified both</p>
<p style="text-align: right;">Page 27</p> <p>1 pharmaceutical company or founders 2 equity, I can't do experiments in my 3 laboratory. That's considered to be a 4 conflict of interest at our institution. 5 And most reputable institutions that I 6 have experience with, and Canada. 7 Q. So you receive only public 8 funding in your lab? 9 A. I have -- at the present 10 time? At the present time all of my 11 funding is public or startup funding for 12 my institution. 13 Q. How about at any time? 14 A. When I was at Princess 15 Margaret Cancer Centre in Toronto, which 16 was my second job, I received a -- a 17 grant from Novartis Pharmaceuticals to do 18 studies related to the possible uses of 19 SHIP2 inhibitors, which I'm an expert in, 20 in cancer. So that was a two-year grant 21 that had specific aims and milestones and 22 reports that I had. And it was more like 23 a pharmaceutical funding grant, but I was 24 not receiving any equity in the company</p>	<p style="text-align: right;">Page 29</p> <p>1 of those molecules. 2 Q. Okay. And that -- and that 3 policy goes for lab funding as well as 4 compensation, correct? 5 A. Which policy? 6 Q. The policy that would be 7 conflict of interest that prohibits you 8 from doing any experiments for 9 remuneration. 10 A. No. The conflict of 11 interest policy is that I can't receive 12 personal compensation. We are allowed to 13 receive some -- we are allowed to 14 pursue 20 -- we're allowed to use 15 20 percent of our time outside of -- of 16 our hospital or medical school time for 17 consulting, expert witnesses, 18 participation in biotechnology companies. 19 That money has to be separate from your 20 lab money. 21 Q. Okay. But there would be 22 nothing that would prevent Johnson & 23 Johnson from providing laboratory funding 24 for -- for research or experiments?</p>

Page 30	Page 32
<p>1 A. There would, if I were 2 receiving compensation, as I am for 3 serving as an expert witness in this 4 case. That would be a conflict in my -- 5 my view of the conflict of interest 6 policy. I didn't consult the -- the 7 hospital about that.</p> <p>8 Q. Okay. And does that same 9 policy apply to anyone in your lab?</p> <p>10 A. Yes.</p> <p>11 Q. What did you know about 12 talcum powder and ovarian cancer before 13 you were approached by Mr. Winter?</p> <p>14 A. I had seen reports in the 15 process of litigation and, you know, 16 that's pretty much it.</p> <p>17 Q. And you had not reviewed any 18 of the literature regarding the issue, 19 correct?</p> <p>20 A. That's correct.</p> <p>21 Q. Did you have any opinions 22 formed at that time?</p> <p>23 A. No.</p> <p>24 Q. May I assume that all of the</p>	<p>1 literature to cite?</p> <p>2 A. Yes.</p> <p>3 Q. And did you choose the 4 quotes that you include in your report?</p> <p>5 A. Yes.</p> <p>6 Q. The references that you 7 cited that are attached to your report, 8 may I assume that those are the ones that 9 you deemed most important relating to 10 your opinions?</p> <p>11 A. Yes.</p> <p>12 Q. Did you perform any 13 searches?</p> <p>14 A. Yes. As I said earlier, I 15 did several searches.</p> <p>16 Q. What terms did you use?</p> <p>17 A. Well, I can't remember all 18 of them in detail, but certainly talc and 19 inflammation. Talc and ovarian cancer. 20 I don't remember all of them. But those 21 are a couple.</p> <p>22 Q. And what's your favorite 23 search engine or site?</p> <p>24 A. I use both Google and PubMed</p>
Page 31	Page 33
<p>1 opinions that you plan to give today are 2 contained in your expert report?</p> <p>3 MS. SHARKO: Object to the 4 form of the question. It depends 5 what you ask him.</p> <p>6 THE WITNESS: Should I 7 answer?</p> <p>8 MS. SHARKO: Yes, you can 9 answer.</p> <p>10 THE WITNESS: How could I 11 say that until I hear what you ask 12 me? I can't answer that.</p> <p>13 BY DR. THOMPSON:</p> <p>14 Q. Or additional opinions that 15 you give in response to my questions. 16 Would that be fair?</p> <p>17 A. Yes.</p> <p>18 Q. Who wrote your expert 19 report?</p> <p>20 A. I did.</p> <p>21 Q. Did you write every word of 22 the expert report?</p> <p>23 A. Yes.</p> <p>24 Q. Did you choose the</p>	<p>1 for different searches. I find them -- 2 they provide different information.</p> <p>3 Q. The -- on the materials 4 considered, Exhibit Number 3, there are a 5 bunch of plaintiff expert reports listed. 6 Did you read all of those?</p> <p>7 A. No.</p> <p>8 Q. Can you go through and tell 9 me which ones you did read?</p> <p>10 A. I read Dr. Saed's report. I 11 read Dr. Zelikoff's report. And I read 12 Dr. Smith-Bindman's report, and I read is 13 it Dr. -- is it Levy or Levy's report? 14 I'm not sure how to pronounce his name. 15 I'm sorry.</p> <p>16 Q. Any others?</p> <p>17 A. No.</p> <p>18 Q. You did not look at 19 Dr. Crowley's report?</p> <p>20 A. No.</p> <p>21 Q. Why not?</p> <p>22 A. I just didn't think it 23 relevant.</p> <p>24 Q. Do you know what</p>

<p style="text-align: right;">Page 34</p> <p>1 Dr. Crowley's report addressed?</p> <p>2 A. I don't recall. I scanned</p> <p>3 through the intros of all of them. But I</p> <p>4 didn't think it was really relevant.</p> <p>5 Q. Dr. Crowley's report</p> <p>6 addressed the fragrance chemicals in</p> <p>7 Johnson's Baby Powder. Was that not</p> <p>8 relevant for you?</p> <p>9 A. No, not in my opinion.</p> <p>10 Q. And why is that?</p> <p>11 A. Because that wasn't the</p> <p>12 issue that I was asked to address. I was</p> <p>13 asked to address Johnson & Johnson Baby</p> <p>14 Powder studies that used the Baby Powder.</p> <p>15 So what was in them was irrelevant to the</p> <p>16 conclusion. It was just the conclusion,</p> <p>17 the effects that were relevant. And I</p> <p>18 was asked to address the issue of talc</p> <p>19 and ovarian cancer.</p> <p>20 Q. So it doesn't matter to you</p> <p>21 what else is in the Baby Powder?</p> <p>22 A. Not from the standpoint of</p> <p>23 experiments that involve the Baby Powder.</p> <p>24 It's just the results of the Baby Powder.</p>	<p style="text-align: right;">Page 36</p> <p>1 are talking about today, correct?</p> <p>2 A. I don't know. That's -- I</p> <p>3 mean, I considered them for sure.</p> <p>4 Q. Okay. When you say talc are</p> <p>5 you referring to talcum powder?</p> <p>6 A. Yes.</p> <p>7 Q. Are you referring to talcum</p> <p>8 powder that's platy?</p> <p>9 A. I'm referring to the talcum</p> <p>10 powder that was used in the</p> <p>11 epidemiological studies and in the</p> <p>12 experiments of Dr. Saed and others that I</p> <p>13 considered for the purposes of my report.</p> <p>14 I can't give you an exhaustive listing of</p> <p>15 what they use. But I did consider those</p> <p>16 papers in issuing my opinion.</p> <p>17 Q. Well, those are two</p> <p>18 different things. The epidemiology</p> <p>19 studies are typically done calling the</p> <p>20 agent that's being asked about talcum</p> <p>21 powder. And Dr. Saed's experiments were</p> <p>22 specifically done with Johnson's Baby</p> <p>23 Powder, correct?</p> <p>24 MS. SHARKO: Object to the</p>
<p style="text-align: right;">Page 35</p> <p>1 Q. And throughout your report</p> <p>2 you refer to talc. What do you mean by</p> <p>3 that?</p> <p>4 A. I mean talc. What do you</p> <p>5 mean by that?</p> <p>6 Q. Well, is it Baby Powder or</p> <p>7 is it talc?</p> <p>8 A. No -- well, it's -- the talc</p> <p>9 that I referred to is generic talc. It</p> <p>10 could be talc from chemical companies.</p> <p>11 Whatever was used in the experiments in</p> <p>12 the reports that -- and/or the studies</p> <p>13 that I read that were epidemiological</p> <p>14 based.</p> <p>15 Q. What are the products that</p> <p>16 are at issue today in the litigation?</p> <p>17 A. I'm not an expert on what's</p> <p>18 involved in litigation. I know that</p> <p>19 Johnson & Johnson Baby Powder and Baby</p> <p>20 Shower (sic) are involved in the</p> <p>21 litigation. I'm not aware of any other</p> <p>22 specific products that are involved.</p> <p>23 Q. So Johnson Baby Powder and</p> <p>24 Shower to Shower are the products that we</p>	<p style="text-align: right;">Page 37</p> <p>1 form of the question. Lacks</p> <p>2 foundation.</p> <p>3 THE WITNESS: The</p> <p>4 epidemiological studies, in fact,</p> <p>5 were performed using a variety of</p> <p>6 different products. So there</p> <p>7 wasn't a single product used. But</p> <p>8 Johnson & Johnson products were in</p> <p>9 some of them. Some of the studies</p> <p>10 also included cornstarch.</p> <p>11 The Saed studies, as I</p> <p>12 recall, but we have to look at</p> <p>13 them in detail to be sure,</p> <p>14 included talc from chemical</p> <p>15 companies and Johnson & Johnson</p> <p>16 products.</p> <p>17 BY DR. THOMPSON:</p> <p>18 Q. And we will get to</p> <p>19 Dr. Saed's work. Did you see the paper</p> <p>20 that Dr. Saed just published in the last</p> <p>21 few weeks?</p> <p>22 A. I didn't see the final</p> <p>23 version of the paper. But I saw the</p> <p>24 accepted version that was supplied to us</p>

<p style="text-align: right;">Page 38</p> <p>1 after his deposition. And I reviewed 2 that. 3 Q. Why did you not look at the 4 final published paper? 5 A. Because the -- as far as I 6 know, the paper was accepted. So an 7 accepted paper is the same as the 8 published paper. But I'm happy to look 9 at it if you'd like. 10 Q. I'm just asking you why you 11 didn't think that was important to look 12 at yourself. 13 A. Because -- 14 MS. SHARKO: Object to the 15 form of the question. 16 THE WITNESS: Because an 17 accepted paper, in my experience, 18 is identical to the actual paper 19 except for minor editorial, you 20 know, placements of figures and 21 things like that. Once it's 22 accepted, it's not changed. 23 BY DR. THOMPSON: 24 Q. So your opinion is that in</p>	<p style="text-align: right;">Page 40</p> <p>1 which talcum powder may cause or 2 contribute to ovarian cancer, doesn't it 3 make a difference what the components of 4 that talcum powder are? 5 A. No. If I am referring to 6 the papers that are published by experts 7 for the plaintiffs to argue for a 8 pathogenic role, I should be considering 9 what they use. That's the only role of 10 an issue here in my opinion. 11 Q. So if it's shown that talcum 12 powder contains fibrous talc, which is 13 listed as a Group 1 carcinogen by IARC, 14 that would not matter to you in your 15 opinions as to what the mechanism might 16 be for the carcinogenesis of Baby 17 Powder -- 18 MS. SHARKO: Object to 19 the from of the -- 20 BY DR. THOMPSON: 21 Q. -- correct? 22 MS. SHARKO: Object to the 23 form of the question. Lacks 24 foundation.</p>
<p style="text-align: right;">Page 39</p> <p>1 the final accepted paper, there was a 2 discussion of talcum powder other than 3 Johnson's Baby Powder; is that right? 4 A. I don't recall. I'm happy 5 to look at the paper. 6 Q. We'll look at that a little 7 bit later. 8 And does talcum powder 9 include fibrous talc? 10 A. Talcum powder includes what 11 I just said. It's whatever was in the 12 products that were used in the 13 epidemiology studies and whatever was 14 used in any of the individual papers. 15 And I'm happy to go through any single 16 one of them with you and review the 17 details. But I obviously can't remember 18 which products were used in every single 19 epidemiology study that I reviewed and in 20 every single paper that I reviewed, 21 including, you know, papers from Dr. Saed 22 and others. 23 Q. From a molecular standpoint, 24 here to testify about the mechanism by</p>	<p style="text-align: right;">Page 41</p> <p>1 THE WITNESS: Can you repeat 2 the question, please? 3 BY DR. THOMPSON: 4 Q. So if it's shown that talcum 5 powder contains fibrous talc, which is 6 listed as a Group 1 carcinogen by IARC, 7 that would not matter to you in your 8 opinions as to what the mechanism might 9 be, correct? 10 A. Yes. That's correct. 11 Because my opinion is based on the 12 studies that involved the application of 13 talc, including Johnson & Johnson 14 products, perineally, and also in some 15 cases injected and applied to cells. And 16 that would -- if, you know, the products 17 have any substance in them, then they 18 should have revealed a carcinogenic 19 effect in those studies or they should 20 have revealed something supporting the 21 plaintiffs' experts arguments. But I 22 found no evidence that that's the case. 23 None. 24 Q. Are you speaking of</p>

<p style="text-align: right;">Page 42</p> <p>1 epidemiological evidence?</p> <p>2 A. I'm speaking of every -- of</p> <p>3 all of the evidence that I covered in my</p> <p>4 report. And I'm happy to go through any</p> <p>5 individual one. But it's all of the</p> <p>6 evidence that I considered in my report.</p> <p>7 I found no compelling scientific evidence</p> <p>8 to support the position that talc causes</p> <p>9 ovarian cancer.</p> <p>10 Q. Okay. We'll get to that a</p> <p>11 little bit more later.</p> <p>12 And you did not look at</p> <p>13 Dr. Longo's reports, correct?</p> <p>14 A. That's correct.</p> <p>15 Q. And for the same reason that</p> <p>16 you did not consider it relevant to your</p> <p>17 opinions?</p> <p>18 A. Correct.</p> <p>19 Q. And do you know what</p> <p>20 Dr. Longo's report addressed?</p> <p>21 A. I don't recall. As I told</p> <p>22 you I scanned through each of them to</p> <p>23 decide which ones I should look at in</p> <p>24 more detail.</p>	<p style="text-align: right;">Page 44</p> <p>1 Q. Do you know who Dr. David</p> <p>2 Kessler is?</p> <p>3 A. I don't recall.</p> <p>4 Q. And you have listed</p> <p>5 references to various websites. What was</p> <p>6 the purpose for selecting these websites</p> <p>7 to include on your materials considered?</p> <p>8 A. Well, there were different</p> <p>9 purposes for different websites. Do you</p> <p>10 want to walk through them one by one?</p> <p>11 Q. No, we'll get back to some</p> <p>12 of them I think.</p> <p>13 Did you list any websites</p> <p>14 that did identify a risk of ovarian</p> <p>15 cancer with the perineal use of talcum</p> <p>16 powder products?</p> <p>17 A. I don't recall what's in</p> <p>18 every one of the websites, but I don't</p> <p>19 believe so.</p> <p>20 Q. You are aware that there are</p> <p>21 websites that would list talcum powder</p> <p>22 use as a risk factor for ovarian cancer,</p> <p>23 correct?</p> <p>24 A. I'm not aware of what</p>
<p style="text-align: right;">Page 43</p> <p>1 Q. So you were not aware that</p> <p>2 Dr. Longo actually tested a number of</p> <p>3 Baby Powder and Shower to Shower samples</p> <p>4 from Johnson & Johnson over decades when</p> <p>5 they were produced, correct?</p> <p>6 A. Correct.</p> <p>7 MS. SHARKO: Object to the</p> <p>8 form of the question.</p> <p>9 BY DR. THOMPSON:</p> <p>10 Q. And you did not look at any</p> <p>11 of the GYN oncology reports, correct?</p> <p>12 That would be Dr. Daniel</p> <p>13 Clarke-Pearson, Dr. Ellen Blair Smith or</p> <p>14 Dr. Judy Wolf?</p> <p>15 A. That's correct. I -- I</p> <p>16 looked through them -- I looked at the --</p> <p>17 at the general, you know, statements in</p> <p>18 the beginning and decided they weren't</p> <p>19 really relevant to my expertise.</p> <p>20 Therefore, I didn't look at them in</p> <p>21 detail.</p> <p>22 Q. Did you read the expert</p> <p>23 report of Dr. David Kessler?</p> <p>24 A. No.</p>	<p style="text-align: right;">Page 45</p> <p>1 websites that I didn't look at say. I'm</p> <p>2 aware of what websites that I did look at</p> <p>3 say.</p> <p>4 Q. So you did not see any</p> <p>5 websites that listed talcum powder use as</p> <p>6 a risk factor; is that correct?</p> <p>7 Or you don't know one way or</p> <p>8 the other?</p> <p>9 A. I don't recall if I did or I</p> <p>10 didn't.</p> <p>11 Q. And you reviewed IARC 2010,</p> <p>12 correct?</p> <p>13 A. Correct.</p> <p>14 Q. And what is IARC?</p> <p>15 A. International Agency For</p> <p>16 Research and Cancer, I believe.</p> <p>17 Q. And what is the subject</p> <p>18 matter of the monograph from 2010?</p> <p>19 A. It covers several things. I</p> <p>20 don't remember the exact details, but</p> <p>21 we -- I can look it up.</p> <p>22 Q. We'll come back to it.</p> <p>23 And is it your understanding</p> <p>24 that the IARC 2010 monograph reviewed</p>

<p style="text-align: right;">Page 46</p> <p>1 literature as of 2006, correct?</p> <p>2 A. I can't recall in detail</p> <p>3 when they cut off the literature.</p> <p>4 Q. We'll look at that.</p> <p>5 And you are aware that the</p> <p>6 IARC monograph in 2010, published,</p> <p>7 reviewing literature up to 2006,</p> <p>8 specifically dealt with non-asbestiform</p> <p>9 talc, correct?</p> <p>10 A. That's my recollection. But</p> <p>11 again, I read that a while ago. And I'm</p> <p>12 happy to go back and look at it with you</p> <p>13 if you want to jog my memory.</p> <p>14 Q. That's a pretty important</p> <p>15 fact, don't you think?</p> <p>16 A. It's not material to the</p> <p>17 question at hand as far as I can tell.</p> <p>18 Because as, again, I was asked to review</p> <p>19 the issue of, you know, Johnson & Johnson</p> <p>20 products and/or talc and ovarian cancer</p> <p>21 with respect to the evidence in the</p> <p>22 scientific literature as to its</p> <p>23 carcinogenicity, and that's what I</p> <p>24 reviewed. And whatever talc was used in</p>	<p style="text-align: right;">Page 48</p> <p>1 suppliers like -- chemical suppliers like</p> <p>2 Sigma.</p> <p>3 And each study is different.</p> <p>4 But the -- the studies that I cited in my</p> <p>5 report all used various forms of "talc"</p> <p>6 and that's what I considered in offering</p> <p>7 my opinion.</p> <p>8 Q. You'll agree that the</p> <p>9 molecular studies identified where the</p> <p>10 talc came from or the talcum powder came</p> <p>11 from, correct?</p> <p>12 A. Yes.</p> <p>13 Q. The epidemiological studies</p> <p>14 typically do not, correct?</p> <p>15 A. I don't believe that that is</p> <p>16 correct. Some of them say specifically</p> <p>17 what products they are. And some of them</p> <p>18 are not as specific. So it's not a</p> <p>19 one-size-fits-all for that question.</p> <p>20 Q. Are you aware of an</p> <p>21 epidemiological study that actually</p> <p>22 refers to what actual product was used by</p> <p>23 the women included in the study?</p> <p>24 A. My recollection is several</p>
<p style="text-align: right;">Page 47</p> <p>1 those studies would have, you know, been</p> <p>2 the relevant talc. So that's what I</p> <p>3 reviewed.</p> <p>4 Q. So studies that were --</p> <p>5 would address asbestos and ovarian cancer</p> <p>6 are not relevant?</p> <p>7 A. Not insofar as I can tell.</p> <p>8 Because I was looking at the issue of</p> <p>9 Johnson & Johnson products and/or talc as</p> <p>10 defined by the authors of the papers that</p> <p>11 used these materials, and/or the authors</p> <p>12 of the epidemiological studies that</p> <p>13 studied this issue on -- in offering my</p> <p>14 opinion.</p> <p>15 Q. And you are talking about</p> <p>16 the epidemiological studies, correct?</p> <p>17 A. No. I'm talking about the</p> <p>18 epidemiological studies which used</p> <p>19 certain things. And then I'm talking</p> <p>20 about the bio -- biological studies such</p> <p>21 as they are, that used various forms of</p> <p>22 talc, whether it's Johnson -- in some</p> <p>23 case it's Johnson & Johnson products</p> <p>24 directly. In other cases, talc from</p>	<p style="text-align: right;">Page 49</p> <p>1 said Johnson & Johnson's products. But</p> <p>2 we'd have to go through all of the</p> <p>3 24-case-control studies and three cohort</p> <p>4 studies that I looked at.</p> <p>5 Q. Do you know what Johnson &</p> <p>6 Johnson's market share of Baby Powder has</p> <p>7 been over the years?</p> <p>8 A. I have no idea.</p> <p>9 Q. You also reviewed the IARC</p> <p>10 monograph in 2012, correct?</p> <p>11 A. Which one is that?</p> <p>12 Q. That's the one related to</p> <p>13 asbestos.</p> <p>14 A. I looked at that very</p> <p>15 cursorily. I really didn't have the time</p> <p>16 to do an exhaustive study of asbestos and</p> <p>17 ovarian cancer. I looked at it</p> <p>18 cursorily. And several other papers.</p> <p>19 Q. And even if Johnson &</p> <p>20 Johnson's Baby Powder and Shower to</p> <p>21 Shower have -- are shown to contain</p> <p>22 asbestos, that was -- reviewing that</p> <p>23 evidence and that data were not</p> <p>24 important?</p>

<p style="text-align: right;">Page 50</p> <p>1 A. No, because the issue is 2 whether there is any compelling 3 scientific evidence that Johnson & 4 Johnson's products, when applied 5 perineally, give rise to an increased 6 incidence of ovarian cancer, and/or 7 whether there was any evidence that 8 Johnson & Johnson products, when applied 9 in experimental animals have any evidence 10 of causing pre or neoplastic conditions 11 of the ovaries or fallopian tubes. 12 That was the issue that I 13 considered in issuing my report. And 14 therefore, the issue is what's -- what 15 the Johnson & Johnson products do, not 16 whether asbestos is involved in ovarian 17 cancer. 18 Q. Are you aware of animal 19 studies that use Johnson & Johnson Baby 20 Powder? 21 A. I would have to go back and 22 look at the actual studies to see what 23 was used in those studies. 24 Q. You don't know that?</p>	<p style="text-align: right;">Page 52</p> <p>1 But I didn't have a chance to study it in 2 any detail. 3 Q. You didn't ask -- 4 A. In any event, it's a draft, 5 so it hasn't been, you know, finalized. 6 So I don't really think it's relevant 7 until it's finalized. 8 Q. Well, do you know anything 9 about the policy that Health Canada 10 follows to publish a draft to open up for 11 comments -- 12 A. No. 13 Q. -- before it's finalized? 14 A. No. 15 Q. Did you review the 16 conclusions of the Health Canada risk 17 assessment draft that you were provided 18 yesterday? 19 A. Not in -- I didn't have time 20 really to review it in any significant 21 detail. So the answer to that is no. 22 But I'm happy to do it now. 23 Q. Well, you know you referred 24 to the Health Canada risk assessment</p>
<p style="text-align: right;">Page 51</p> <p>1 A. I don't remember. 2 Q. That wasn't something that 3 would have been important? 4 A. I read through all of the 5 animal studies, none of which show any 6 significant carcinogenic effect of talc 7 that was used in the studies. 8 Q. We'll get to those. 9 You reviewed the Health 10 Canada risk assessment, correct? 11 A. Are we talking about the 12 Taher, et al., paper? 13 Q. No, we are talking about the 14 risk assessment published by -- draft 15 published by Health Canada. 16 A. I haven't actually read the 17 draft. 18 Q. Why not? 19 A. I haven't seen it. 20 Q. So you were not provided the 21 Health Canada risk assessment? 22 A. I was given -- you know, 23 yesterday, you know, the lawyers showed 24 me briefly there was a health assessment.</p>	<p style="text-align: right;">Page 53</p> <p>1 draft in your report? 2 A. No, not that I recall. 3 Where do I refer -- I refer to the Taher, 4 et al., paper which was the basis for the 5 study that was being done at Health 6 Canada. 7 Q. How do you know that the 8 Taher paper was the basis for the Health 9 Canada risk assessment? 10 A. I think it says it in the 11 paper. 12 Q. Okay. We'll get to that 13 when we get to that section. 14 And you reviewed an FDA 15 letter in response to a citizen's 16 petition, correct? 17 A. Yes. 18 Q. And was that provided to you 19 by counsel? 20 A. Yes. 21 (Document marked for 22 identification as Exhibit 23 Neel-4.) 24 BY DR. THOMPSON:</p>

<p style="text-align: right;">Page 54</p> <p>1 Q. I've marked as Exhibit 4 2 Appendix A to your report. And just tell 3 me what this is. 4 A. This is a list -- 5 MS. SHARKO: Just take your 6 time and look through it. 7 THE WITNESS: This is a list 8 of the most recent genome-wide 9 association studies. That show 10 genome-wide association -- that 11 show association with specific 12 single-nucleotide polymorphisms 13 with increased risk of ovarian 14 cancer. 15 BY DR. THOMPSON: 16 Q. And how does something make 17 it to the -- this list? 18 A. How does it make it to this 19 list? When there's been a -- any 20 publication of a genome-wide association 21 study is aggregated. 22 Q. And so that's when there 23 have been enough studies published on a 24 certain gene to reach statistical</p>	<p style="text-align: right;">Page 56</p> <p>1 THE WITNESS: I wasn't done. 2 BY DR. THOMPSON: 3 Q. Sorry. 4 A. So some of -- you know, the 5 ones that are over 10-8 are the only ones 6 that can be considered as documented risk 7 SNPs. 8 Q. And there are new SNPs being 9 reported all the time. You would agree 10 with that, correct? 11 A. Well, the SNPs aren't being 12 reported. The SNPs have pretty much -- 13 you know, the SNPs that are used in the 14 genome-wide association studies are the 15 SNPs that are on standard panels. 16 What do you mean new SNPs 17 being reported all the time? There are 18 private SNPs between any two individuals. 19 If I sequence you and I sequence me, we 20 might find, you know, a new 21 single-nucleotide polymorphism. But 22 that's a privacy SNP for you or for me. 23 It's not one of the ones that was used to 24 map genes.</p>
<p style="text-align: right;">Page 55</p> <p>1 significance, correct? 2 A. Yes. Well, the statistical 3 significance of each -- well, there's 4 different levels of statistical 5 significance in the GWAS for every 6 location that's cited in the GWAS. So 7 some of them are -- and if you go on the 8 website and look at it, you'll see that 9 it lists the P-value for every 10 association. 11 So some of them have reached 12 genome-wide significance, and some of 13 them haven't. So the ones that are 14 believed to be documented associations 15 are those that have reached genome-wide 16 significance. And that means that they 17 have less than 10-8. There are other 18 genome-wide association snips that have 19 reached less than 10-8. 20 Q. And there are snips -- 21 MS. SHARKO: Wait, wait, 22 wait. 23 Are you done with your 24 answer?</p>	<p style="text-align: right;">Page 57</p> <p>1 Q. Right. I understand that. 2 But there is ongoing research in this 3 area, correct? 4 A. Yes, there's ongoing 5 research in genetic basis of all cancers. 6 (Document marked for 7 identification as Exhibit 8 Neel-5.) 9 BY DR. THOMPSON: 10 Q. Exhibit 5 is your CV. It 11 appears that that was updated 12 February 22nd, 2019, correct? 13 A. Yes. 14 Q. And you have quite a few 15 publications, I see. 16 A. Not as many as I'd like. 17 Q. Well, you still have a lot 18 of time, right, in your career, I hope. 19 How -- how many of these 20 deal with ovarian cancer? 21 A. I don't know. We can go 22 through each of them. I don't know 23 offhand. 24 Q. Does eight sound about</p>

<p style="text-align: right;">Page 58</p> <p>1 right?</p> <p>2 A. I can count them. Possibly</p> <p>3 eight. But you know, cancer biology is</p> <p>4 much more broad than a specific cancer.</p> <p>5 So, I mean, my expert opinion is based on</p> <p>6 30 years of research, actually more than</p> <p>7 30. 30 years as a faculty member at</p> <p>8 Harvard Medical School, Princess Margaret</p> <p>9 and now NYU. And before that, you know,</p> <p>10 graduate school and Ph.D. and post-doc --</p> <p>11 Ph.D. and post-doc training. So I've had</p> <p>12 about 36 years of -- no, 39 years of --</p> <p>13 wow, that's a lot of time -- 39 years of</p> <p>14 research experience in this field.</p> <p>15 From the earliest days of</p> <p>16 the cancer biology field, I was involved</p> <p>17 in, you know, some of the earliest major</p> <p>18 discoveries that led to the molecular age</p> <p>19 of cancer.</p> <p>20 Q. And obviously that</p> <p>21 experience with other types of cancer are</p> <p>22 relevant to the study of ovarian cancer</p> <p>23 and the type -- subtypes, correct?</p> <p>24 A. I think so, yes.</p>	<p style="text-align: right;">Page 60</p> <p>1 amplification, certain forms of KRAS</p> <p>2 mutations, certain forms of BRAF</p> <p>3 mutations.</p> <p>4 There's actually drugs in</p> <p>5 the clinic now that are trying to target</p> <p>6 this agent, this -- this molecule.</p> <p>7 It's also mutated in a</p> <p>8 germ -- under a germ-line mutations in a</p> <p>9 disease called Noonan syndrome. And</p> <p>10 we've done a lot of the work on that.</p> <p>11 And there are also different germ-line</p> <p>12 mutations in the disease cause Noonan</p> <p>13 syndrome with multiple lentigines. We've</p> <p>14 done a lot of work on that. We did the</p> <p>15 first mouse models for both of those</p> <p>16 disorders.</p> <p>17 We discovered that there's a</p> <p>18 third type of mutation in SHIP2 or PTPN11</p> <p>19 that causes metachondromatosis, which is</p> <p>20 a rare cancer of the bone. We discovered</p> <p>21 that SHIP2 acts as tumor suppressor gene</p> <p>22 in that.</p> <p>23 So our lab is working a lot</p> <p>24 on using -- on figuring out how to best</p>
<p style="text-align: right;">Page 59</p> <p>1 Q. Are there any articles on</p> <p>2 your CV that relate directly to talcum</p> <p>3 powder and potential carcinogenesis?</p> <p>4 A. No.</p> <p>5 Q. Are there any articles on</p> <p>6 your CV that relate to asbestos?</p> <p>7 A. No.</p> <p>8 Q. Are there any articles on</p> <p>9 your CV that relate to particles of any</p> <p>10 kind?</p> <p>11 A. No.</p> <p>12 Q. Describe for me the</p> <p>13 research -- understanding it's a big lab,</p> <p>14 but generally speaking, what type of</p> <p>15 research is your lab currently doing?</p> <p>16 A. Well, it's divided into</p> <p>17 three main areas. One area has to do</p> <p>18 with SHIP2, which we discussed --</p> <p>19 discovered, which is a critical component</p> <p>20 of growth factor receptor, cytokine</p> <p>21 receptor, and integrin signaling pathways</p> <p>22 and is critical for the transduction of</p> <p>23 signals from activated oncogenes, such as</p> <p>24 the receptor tyrosine kinase</p>	<p style="text-align: right;">Page 61</p> <p>1 deploy SHIP2 inhibitors in the -- in the</p> <p>2 clinic and how to combine them with other</p> <p>3 agents. So that's about a third.</p> <p>4 And then we have a third of</p> <p>5 the lab that's working on ovarian cancer,</p> <p>6 pathogenesis, including studies related</p> <p>7 to the cell of origin, studies related to</p> <p>8 the heterogeneity in ovarian cancer using</p> <p>9 the single cell RNA sequencing, and</p> <p>10 various type of single cell RNA FISH.</p> <p>11 And then we have a fourth --</p> <p>12 sorry, a third part of the lab, which</p> <p>13 is -- oh, I forgot. I'm sorry.</p> <p>14 And then we've also</p> <p>15 developed novel organoid systems for both</p> <p>16 the fallopian tube and the ovarian</p> <p>17 surface epithelium in the mouse. And</p> <p>18 we're using that -- those models to</p> <p>19 engineer in the specific mutations that</p> <p>20 have been found in ovarian -- human</p> <p>21 ovarian cancer so we can develop</p> <p>22 syngeneic mouse models to study how to</p> <p>23 best treat these tumors using</p> <p>24 combinations of targeted agents and</p>

<p style="text-align: right;">Page 62</p> <p>1 immunotherapy, including platinum PARP 2 inhibitors, trying to figure out how 3 cyclin E tumors can be treated since 4 they're not treated by platinum very 5 well.</p> <p>6 And then the third area of 7 the lab has to do with another 8 phosphatase that we discovered or that we 9 cloned. We didn't discover it. We were 10 the first to clone it, called PPM1 or 11 PP1B. And we're working on how that's 12 involved in breast cancer pathogenesis 13 by -- and in particular how it 14 regulates -- how -- how knocking down or 15 inhibiting PP1B sensitizes breast cancer 16 cells, or certain types of breast cancer 17 cells, to hypoxia using -- and in 18 particular, how the -- there is an 19 interaction between this PP1B and this 20 novel E3 ligase called RNF213, which is 21 the disease gene for moyamoya syndrome 22 which is a very rare syndrome that causes 23 precocious strokes in children.</p> <p>24 So that's the -- that's the</p>	<p style="text-align: right;">Page 64</p> <p>1 About 50 of which are genomically 2 characterized, and we are collaborating 3 with people to use those.</p> <p>4 And we are sometimes 5 making -- we also make organoid -- we're 6 working on organoid systems from humans. 7 So we get tissues from our Winthrop 8 colleagues. And that's under an IRB 9 protocol, so -- but we don't do any 10 clinical trials.</p> <p>11 I'm consulting on a clinical 12 trial that has to do with a different 13 area of research that we transiently were 14 involved in that's distantly related to 15 the moyamoya syndrome thing. I don't 16 know that you want to go into that, but 17 I'm happy to discuss that.</p> <p>18 Q. Probably not.</p> <p>19 A. Has to do with -- has to do 20 with vitamin --</p> <p>21 MS. SHARKO: Let him finish.</p> <p>22 THE WITNESS: Has to do with 23 vitamin C and the connection 24 between vitamin C and this pathway</p>
<p style="text-align: right;">Page 63</p> <p>1 major work being done in the lab.</p> <p>2 Q. In a nutshell, right?</p> <p>3 A. Yes.</p> <p>4 Q. Does your lab do both in 5 vitro and in vivo animal model research?</p> <p>6 A. Yes.</p> <p>7 Q. Do you do human research?</p> <p>8 A. What do you mean by human 9 research?</p> <p>10 Q. Anything that requires an 11 IRB, approval, the biomarkers in 12 patients, anything of that sort?</p> <p>13 A. We have -- so IRB approval 14 is required to get issues and it's 15 usually a pretty standard -- what they 16 call administrative approval. So if 17 you're counting that, yes, we have 18 approval to get the tissues that we use 19 to make ovarian cancer xenographs.</p> <p>20 We have a variety -- I 21 forgot to mention that we have a large 22 collection of ovarian cancer xenographs 23 in the lab that mainly came from my time 24 in Toronto. So we have hundreds of them.</p>	<p style="text-align: right;">Page 65</p> <p>1 that I mentioned to you of PP1B 2 and RNF213.</p> <p>3 And we -- in reading the 4 literature on that, I realized 5 that there was a possible use of 6 vitamin C in myeloid dysplastic 7 syndrome and AML, and we got 8 together with some of my other 9 colleagues upstairs and did a 10 major paper that was published in 11 Cell last year and led to a 12 clinical trial.</p> <p>13 So I'm helping the junior 14 faculty member in my department to 15 design that trial and to execute 16 it, which is running at the cancer 17 center right now.</p> <p>18 So that's the only 19 connection. But I'm actually not 20 on that IRB, because I'm not 21 really doing the study.</p> <p>22 BY DR. THOMPSON:</p> <p>23 Q. Okay. And I -- I am not 24 intentionally interrupting you.</p>

<p style="text-align: right;">Page 66</p> <p>1 Sometimes it's hard to tell when there's 2 a pause. Just so -- 3 A. I have to catch my breath, 4 you know. 5 Q. -- so you know that. 6 And the tissue samples that 7 you use, is that something that some 8 would refer to as ex vivo research? 9 A. So, you know, the use of the 10 word ex vivo is used pretty sloppily in 11 literature. Including some e-mails -- I 12 actually think it's confusing when to use 13 in vivo and not -- when to use in -- some 14 people use in vivo to refer to mice, to 15 mouse experiments. Some people don't. 16 Some people use in vivo 17 to -- some people -- I think what we can 18 all agree on is in vitro -- if it's a 19 pure biochemistry experiment where there 20 are no cells, that's in vitro. 21 Some people would then call 22 putting the same, you know, testing 23 agents on cells in vitro. Some would 24 call it in vivo.</p>	<p style="text-align: right;">Page 68</p> <p>1 going to shut down completely in two 2 months. 3 So if you call those ex 4 vivo, then that's ex vivo. But it's very 5 confusing nomenclature. So I prefer to 6 explain what we're actually doing, and 7 then you can judge what you want to call 8 it. 9 Q. And I'm glad to know I'm not 10 the only one that's confused, so... 11 A. I think it's sloppy, sloppy 12 wording. 13 Q. And you have published with 14 immortalized cell lines, correct? 15 A. Yes. 16 Q. As of most researchers in 17 the -- that are doing in vitro research, 18 correct? 19 A. Yes, but I -- the context is 20 important. And, you know, it's like -- 21 you use the right -- you have to -- if 22 you want to get definitive results or 23 interpretable results or convincing 24 results, you have to use the right cell</p>
<p style="text-align: right;">Page 67</p> <p>1 And ex vivo, some people 2 would call taking cell -- taking human 3 cells out and doing the same kind of 4 studies that other people call in vitro. 5 So I can say what we do. 6 We -- as I told you, we make 7 organoids, which are these culture 8 systems that allow you to basically grow 9 the cells in much more physiologically 10 relevant settings involving extracellular 11 matrix and they form glands and things 12 like that. 13 We make organoids from 14 fallopian tube, from ovarian surface 15 epithelium of the mouse. And we have 16 done more limited work on making 17 fallopian tube organoids from the human. 18 We also have been involved 19 in studies, some of which will come out 20 soon in Nature Medicine, on the use -- on 21 developing organoid conditions for 22 culturing human ovarian cancers. And we 23 did that in my Toronto lab, which is 24 almost completely shut down. They are</p>	<p style="text-align: right;">Page 69</p> <p>1 system for the right experiment at the 2 right time. That's the point. 3 Q. What is contained in 4 Johnson's Baby Powder in your mind? 5 A. I -- I have no knowledge as 6 to what's in Johnson & Johnson's Baby 7 Powder. I'm not a chemist. I'm not a, 8 you know, material scientist, so... 9 Q. Do you even know what's on 10 the bottle as to what is contained? 11 A. No. 12 Q. And that doesn't matter to 13 you? 14 A. Not for the purpose of 15 writing my report, no. Or for examining 16 any of the studies that I referred to in 17 my report, no. It doesn't. 18 Q. Okay. And -- and would you 19 give the same answers for the Shower to 20 Shower product? 21 A. Yes. 22 Q. And it's your understanding 23 that Johnson & Johnson owns and 24 manufactures Johnson's Baby Powder,</p>

Page 70	Page 72
<p>1 correct?</p> <p>2 MS. SHARKO: Object to the</p> <p>3 form of the question. Lacks</p> <p>4 foundation.</p> <p>5 THE WITNESS: So I have no</p> <p>6 idea what the business structure</p> <p>7 is that gives rise to Johnson &</p> <p>8 Johnson's Baby Powder.</p> <p>9 BY DR. THOMPSON:</p> <p>10 Q. Okay.</p> <p>11 A. All I know is that it's</p> <p>12 called Johnson & Johnson's Baby Powder.</p> <p>13 Q. Okay. And same answer for</p> <p>14 Shower to Shower?</p> <p>15 A. Yes.</p> <p>16 Q. Are you familiar with the</p> <p>17 various grades of talc?</p> <p>18 A. Not in any detail. I'm not</p> <p>19 a geologist.</p> <p>20 Q. And same answer that that</p> <p>21 doesn't -- isn't important to you as far</p> <p>22 as your opinions go in this case?</p> <p>23 A. No, because that wasn't what</p> <p>24 I was addressing in my report, nor what</p>	<p>1 would not know whether those claims would</p> <p>2 be misleading or not, correct?</p> <p>3 MS. SHARKO: Object to the</p> <p>4 form. Lacks foundation.</p> <p>5 THE WITNESS: No, I wouldn't</p> <p>6 have any knowledge of that.</p> <p>7 BY DR. THOMPSON:</p> <p>8 Q. Is it important for you to</p> <p>9 know the mineral content of a talcum</p> <p>10 powder product?</p> <p>11 A. Not for the purposes of my</p> <p>12 report, no.</p> <p>13 Q. Would it be important for</p> <p>14 you to know whether there are fibers or</p> <p>15 not in a talcum powder product to assess</p> <p>16 the potential health effects?</p> <p>17 A. Not for the purposes of my</p> <p>18 report which were to look at the specific</p> <p>19 issues that I've already covered.</p> <p>20 Q. And that goes for the</p> <p>21 opinions that you're giving today as</p> <p>22 well?</p> <p>23 A. Absolutely. Mm-hmm. My</p> <p>24 opinions that I'm giving today are based</p>
Page 71	Page 73
<p>1 I'm here to tell you about.</p> <p>2 Q. Do you know anything</p> <p>3 regarding the particle size of Johnson's</p> <p>4 Baby Powder or Shower to Shower?</p> <p>5 A. No.</p> <p>6 Q. Is it important for you to</p> <p>7 know the quality of a talcum powder</p> <p>8 product to assess its talc -- its health</p> <p>9 effects?</p> <p>10 A. No, not for the purpose of</p> <p>11 my report.</p> <p>12 Q. And would you describe</p> <p>13 quality as to the amount of and type of</p> <p>14 impurities in the talcum powder?</p> <p>15 A. I wouldn't describe quality</p> <p>16 because I am not qualified to discuss</p> <p>17 quality.</p> <p>18 Q. Does pure talc exist?</p> <p>19 A. I'm not a geologist. I have</p> <p>20 no opinion on that subject. I have no</p> <p>21 knowledge in that area. I'm a cancer</p> <p>22 biologist.</p> <p>23 Q. So if Johnson & Johnson</p> <p>24 makes claims that their talc is pure, you</p>	<p>1 on my report and any questions that you</p> <p>2 ask me.</p> <p>3 Q. So neither the type of</p> <p>4 fibers or the number of fibers is</p> <p>5 important in your -- in providing your</p> <p>6 opinions for us today?</p> <p>7 A. That's correct.</p> <p>8 Q. And you understand that this</p> <p>9 case involves women who use the Johnson &</p> <p>10 Johnson products in the genital area and</p> <p>11 subsequently developed ovarian cancer,</p> <p>12 correct?</p> <p>13 A. I assume so. I haven't read</p> <p>14 the complaint.</p> <p>15 Q. Okay. And when we talk</p> <p>16 about ovarian cancer generally, we're</p> <p>17 referring to epithelial ovarian cancer.</p> <p>18 Would you agree to that?</p> <p>19 A. Who is "we"?</p> <p>20 Q. You and I today.</p> <p>21 A. Yeah. Sure.</p> <p>22 Q. And I understand --</p> <p>23 A. But I don't -- but I don't</p> <p>24 think it's meaningful to talk about</p>

<p style="text-align: right;">Page 74</p> <p>1 epithelial ovarian cancer anymore. 2 Not -- I mean, that entity is too 3 nondescript to be meaningful from a 2019 4 cellular molecular biology perspective. 5 Q. But you understand that that 6 is done in literature being published 7 every single day? 8 A. It's not done by people who 9 are familiar with the relevant molecular 10 and cellular data. There's lots of 11 papers published that aren't very good. 12 Q. And understanding that there 13 are different histologic types, as well 14 as the -- Type 1 and Type 2 being 15 described. And the field is obviously 16 evolving. Would you agree? 17 A. There were several -- 18 Q. There were. 19 A. Can you make it a more 20 specific question there? 21 Q. Yeah. 22 A. Because I don't necessarily 23 agree with everything that you said. So 24 if you break it down, maybe I can help</p>	<p style="text-align: right;">Page 76</p> <p>1 pretty much settled. But... 2 Q. But there is some debate 3 still as far as whether that applies to 4 some -- some ovarian cancers or all 5 ovarian cancers? 6 A. Well, all cancers have a 7 cell of origin. So I'm not clear what 8 your question is. 9 Q. Bad question. We'll move 10 on. 11 And there is certainly more 12 work being done with the histologic 13 subtypes and whether that's still a good 14 classification system, right? 15 A. I don't think that there is 16 any disagreement among modern ovarian 17 cancer researchers at the top 18 institutions and who are up on the 19 literature as to the fact that it's 20 nonmeaningful to talk about all ovarian 21 cancer or all epithelial ovarian cancer 22 any more than it's legitimate to talk 23 about all breast cancer or all many 24 different types -- lung cancer.</p>
<p style="text-align: right;">Page 75</p> <p>1 get this. 2 Q. I think that's a good 3 criticism of that question. 4 The study of ovarian cancer 5 is an evolving field. Would you agree to 6 that? 7 A. Yes. 8 Q. And in fact, just a couple 9 years ago, National Academy of Science 10 Medicine and Engineering, supported by 11 CDC, sponsored a comprehensive study 12 entitled "Evolving Paradigms in Ovarian 13 Cancer." Are you familiar with that? 14 A. I remember reading it. 15 There's lots of review and things like 16 that. But yeah. 17 Q. And some of the areas that 18 are evolving would be the cell of origin 19 for ovarian -- epithelial ovarian cancer, 20 correct? 21 A. Yes. 22 Q. That's one of the things 23 that your lab is working on? 24 A. Yes. Although we think it's</p>	<p style="text-align: right;">Page 77</p> <p>1 They are separate molecular 2 diseases. Cancer is not a single 3 disease. Ovarian cancer is not a single 4 disease. And it's simply not meaningful 5 to talk about ovarian cancer or even 6 epithelial ovarian cancer. 7 In fact, I would say -- and 8 I would probably be going a little far, 9 but I would probably say that it's no 10 more meaningful to talk about ovarian 11 cancer as an entity than it is to 12 separate epithelial ovarian cancer from 13 germ cell cancers. They're different 14 cells of origin and they have different 15 molecular defects. 16 Q. How about at the patient 17 care level? 18 A. Well, that's one of the 19 problems at the patient care level, is 20 the patient care level hasn't caught up 21 with the molecular biology. And that's 22 the whole goal that what we're doing, 23 because it is ridiculous, in my opinion 24 to treat all ovarian cancer patients the</p>

<p style="text-align: right;">Page 78</p> <p>1 same, and that's why we're not very good 2 at treating it.</p> <p>3 Q. But there is still evolution 4 and debate in the field. Wouldn't you 5 agree?</p> <p>6 MS. SHARKO: Object to the 7 form.</p> <p>8 BY DR. THOMPSON:</p> <p>9 Q. If we -- let's get out of 10 the molecular researchers at an elite 11 university and talk about medical or 12 gynecologic oncologists. You agree that 13 there is going to be a lag time between 14 what you're discovering and how that new 15 novel information gets transmitted and 16 utilized by doctors in the field?</p> <p>17 MR. LOCKE: Objection to 18 form.</p> <p>19 BY DR. THOMPSON:</p> <p>20 Q. Correct?</p> <p>21 A. So that's not -- I agree 22 that there's almost always a lag between 23 laboratory studies and implementation in 24 the clinic. I think that that's not a</p>	<p style="text-align: right;">Page 80</p> <p>1 having talked to women about how they use 2 talcum powder products in the perineal 3 area?</p> <p>4 A. I think I'd get in trouble 5 if I had conversations with women about 6 that. I do have experience in using 7 talcum powder products, however.</p> <p>8 Q. How is that?</p> <p>9 A. When my -- I'm the oldest 10 brother of four boys. And my younger two 11 brothers, you know, are nine and 11 years 12 younger than I am. And as the oldest 13 boy, I was taught to diaper them. And 14 we -- they used -- I used talcum powder 15 products all the time on them. I would 16 dust their bottoms with the talcum powder 17 products.</p> <p>18 Q. Would you currently dust 19 babies with talcum powder knowing what 20 you know?</p> <p>21 A. I don't have any babies, so 22 I haven't given it any thought. I don't 23 have any reason to use it anymore.</p> <p>24 Q. If someone asked you for</p>
<p style="text-align: right;">Page 79</p> <p>1 good thing. And I should point out that 2 I am not just a laboratory researcher, 3 I'm the director of the Perlmutter Cancer 4 Center at NYU Langone. And my job is to 5 try to make sure that research, not just 6 in my lab but in other laboratories in 7 our institution, get translated as 8 quickly as possible in the form of 9 clinical trials at our institution and 10 elsewhere.</p> <p>11 So I think that it is true 12 that modern information has not, you 13 know, transmitted to many people in 14 practice at other institutions.</p> <p>15 But that doesn't mean that 16 the modern information isn't correct.</p> <p>17 Q. And I did not mean to 18 diminish your role at all.</p> <p>19 Do you have any 20 understanding of how the talcum powder 21 products are actually used by women?</p> <p>22 A. I mean, only in the most 23 superficial and vague sense.</p> <p>24 Q. So no firsthand knowledge</p>	<p style="text-align: right;">Page 81</p> <p>1 your advice?</p> <p>2 A. Well, my daughter is 3 pregnant, so maybe I'll have to think 4 about it. But I wouldn't give any advice 5 on that. I'm not -- I'm not a medical 6 doctor. I don't really have any -- 7 everything is different about how diaper 8 goes now.</p> <p>9 We used to use all kinds of 10 different stuff. I don't really remember 11 the details. But, you know --</p> <p>12 Q. So if --</p> <p>13 A. -- I don't remember if we 14 used talc on our girls or not.</p> <p>15 Q. So if your daughter is 16 pregnant knows that you're -- you've 17 looked at this area, serving as an expert 18 for Johnson & Johnson, and asked you if 19 it was safe, would you recommend that she 20 use Johnson's Baby Powder with her new 21 baby, what would you tell her?</p> <p>22 MR. LOCKE: Objection.</p> <p>23 THE WITNESS: Well, my 24 daughter is -- can I answer that?</p>

Page 82	Page 84
<p>1 My daughter who is pregnant 2 is an M.D. Ph.D. student at UCSF 3 and she wouldn't listen to me 4 anyway. 5 BY DR. THOMPSON: 6 Q. Well, that -- 7 A. She's a -- she's got her own 8 opinion. And she's got a Ph.D. in cancer 9 biology herself so she wouldn't -- she 10 would research it herself. So I wouldn't 11 waste the time in telling my daughter who 12 is a Ph.D. at UCSF, which is a better 13 medical school than we have here. 14 Q. Well, that may be true. 15 A. It is true. 16 Q. But if she did ask you, what 17 would you answer? 18 A. I would tell her that she 19 should look into it herself. 20 Q. Okay. And would that be the 21 same if the Baby Powder was shown to 22 contain asbestos? 23 MR. LOCKE: Objection. 24 THE WITNESS: I don't -- as</p>	<p>1 plausibility to those agents 2 causing ovarian cancer. That's 3 the basis of my report. And as I 4 understand it, that's why I am 5 here today, to provide testimony 6 on that basis. 7 BY DR. THOMPSON: 8 Q. And your opinion is there is 9 no biological plausibility to Baby Powder 10 products causing or contributing ovarian 11 cancer in the general sense? 12 A. Yes. I -- that is 13 definitely my opinion. In fact, if 14 anything, there's evidence that it 15 doesn't. 16 There's no evidence that it 17 does. And the available evidence 18 suggests that it doesn't. 19 Q. And you know that talcum 20 powder products are no longer used on 21 condoms or dusting diaphragms, correct? 22 A. I don't know that. 23 Q. Do you know that the FDA has 24 banned powdered medical exam gloves or</p>
Page 83	Page 85
<p>1 I said, I wouldn't give anybody an 2 opinion on that. That's not my 3 place to give people opinions, so 4 it's -- I -- I don't know how to 5 answer your question. 6 BY DR. THOMPSON: 7 Q. Well, you are giving 8 opinions today -- 9 A. I'm giving -- 10 Q. -- as to what women should 11 do, right? 12 MS. SHARKO: Object to the 13 form. 14 THE WITNESS: No. No. 15 MS. SHARKO: Lacks 16 foundation. 17 THE WITNESS: I'm not giving 18 my opinion on what women should 19 do. Women should decide for 20 themselves what they should do. 21 I'm giving an opinion on 22 whether talc or Johnson & 23 Johnson's products, whether 24 there's any biological</p>	<p>1 surgical gloves? 2 MS. SHARKO: Object to the 3 form. Foundation. 4 THE WITNESS: I'm not an 5 expert in regulations that the FDA 6 might have. So I have no reason 7 to know one way or the other, nor 8 why they did it or didn't do it. 9 BY DR. THOMPSON: 10 Q. So in doing your research 11 for your report, was it irrelevant that 12 talcum powder was no longer used on exam 13 gloves or surgical gloves? 14 A. No, that wasn't relevant. 15 Because what I consider for my report was 16 the very clear issue of what, if any, is 17 the role of talcum powder products and/or 18 Johnson & Johnson products that contain 19 talc for ovarian cancer pathogenesis. 20 That was the basis of my 21 report and my reading and researching 22 related to this issue. 23 Q. As a physician would you 24 agree with me that there are no -- no</p>

<p style="text-align: right;">Page 86</p> <p>1 known medical benefits from the use of 2 talcum powder products for hygiene 3 purposes? 4 A. As -- as you established 5 very early, I haven't seen a patient 6 since 1988 so I have no comment on that 7 as a physician. I'm not a -- I'm not a 8 practicing physician. 9 Q. So you don't know one way or 10 the other whether there are any medical 11 benefits? 12 A. I'm not aware of there being 13 any medical benefits. But I'm not in any 14 way current on the literature of, you 15 know, gynecology so -- or any other 16 possible use of talc. So I wouldn't 17 really feel comfortable giving an opinion 18 on something that I'm not an expert on. 19 As opposed to the issue of 20 whether talc causes ovarian cancer, which 21 is right in my area of expertise and I'm 22 quite confident in giving you an opinion 23 on that. 24 Q. Would the average layperson</p>	<p style="text-align: right;">Page 88</p> <p>1 think you told us before that you were 2 aware of some debate or discussion 3 regarding the safety of Baby Powder, did 4 anyone ask you to study that issue? 5 MS. SHARKO: Object to the 6 form. Lacks foundation. 7 THE WITNESS: No one asked 8 me to look at this before 9 Mr. Winter came to me. 10 But, you know, I want to -- 11 I'm not going to agree with the 12 premise of your question, because 13 I wasn't aware of a debate. 14 I think I said that I was 15 aware of reports in the press that 16 there was litigation. That 17 doesn't mean that there's a 18 debate. That just means there's 19 litigation, in my opinion. 20 BY DR. THOMPSON: 21 Q. Fair enough. 22 So prior to the reports in 23 the news over the past few years, you 24 weren't aware of any concerns about Baby</p>
<p style="text-align: right;">Page 87</p> <p>1 know that there are no medical benefits 2 from using Baby Powder? 3 A. I have no idea what the 4 average layperson does. 5 As I say, I don't see 6 patients. So I don't really have any way 7 to assess what the average layperson's 8 knowledge is or isn't of talc products. 9 Q. Would the average layperson 10 understand that there are different 11 molecular subtypes of ovarian cancer? 12 A. Almost certainly not, since 13 I find that many gynecological 14 oncologists don't, you know, in the 15 community. 16 Q. Prior to being contacted 17 regarding serving as an expert in this 18 litigation, did Johnson & Johnson, or 19 anyone for that matter, ever contact you 20 to explore the relationship between 21 talcum powder and ovarian cancer in your 22 laboratory? 23 A. No. 24 Q. And over 39 years, and I</p>	<p style="text-align: right;">Page 89</p> <p>1 Powder in the '70s, '80s, going forward? 2 A. No. I wouldn't -- no. 3 Not -- not -- I only read about things 4 about -- you know, regarding talc since 5 Mr. Winter came to me in May of 2017. 6 Q. And you weren't -- you 7 weren't aware of any concerns about Baby 8 Powder or talcum powder containing 9 asbestos? 10 A. I -- I read things about 11 that in the course of doing my research 12 on this topic. But I wasn't aware of it 13 before. 14 Q. So prior to being consulted, 15 you were not aware of any concerns -- 16 A. Correct. 17 Q. -- about Baby Powder. 18 I think we've answered this. 19 But other than the literature and 20 document review, you have not done any 21 research on the -- on talcum powder and 22 ovarian cancer, correct? 23 A. Just to clarify. I did do 24 one type of research, which is computer</p>

<p style="text-align: right;">Page 90</p> <p>1 research which is in my report. And I 2 want to make sure that I'm not misstating 3 that. 4 I did, you know, for 5 example, test the validity of some of 6 Dr. Saed's claims by just doing simple 7 searches on publicly available websites, 8 some of which were the websites that were 9 cited there. So I don't know if you 10 count that as research. But other than 11 that, no. 12 Q. Okay. Have you discussed 13 your opinions in this case with anyone 14 else? 15 A. No. 16 Q. You have not discussed your 17 opinions with any colleagues? 18 A. None -- I mentioned that I 19 was participating in this case, but other 20 than that I have not discussed my 21 opinions on this -- I probably discussed 22 them with my wife. But that's 23 privileged. 24 Q. I'm not sure it is. But</p>	<p style="text-align: right;">Page 92</p> <p>1 Q. I believe she participated 2 in one of the conferences where -- 3 A. I'm sure she did. 4 Q. -- you were program 5 director? 6 A. I haven't met her 7 personally. I know who she is. 8 Q. Okay. And does that mean 9 that you have not discussed the case with 10 Liz -- Dr. Swisher? 11 A. I have definitely not 12 discussed the case. I don't know. So I 13 couldn't discuss it. 14 Q. I understand. 15 You brought with you today 16 invoices that you had submitted to 17 Johnson & Johnson, correct? 18 A. I didn't bring anything with 19 me today. 20 Q. Someone did. 21 A. Okay. 22 Q. But let me give you a copy 23 of the invoice marked as Exhibit 6. 24 (Document marked for</p>
<p style="text-align: right;">Page 91</p> <p>1 we'll -- we'll give you a pass on that 2 one. 3 A. Okay. Actually I was asked 4 by -- last night, my -- there were people 5 in my house, and I said I can't discuss 6 this, so -- she told me I had to go to 7 sleep. 8 Q. You told -- you mentioned 9 that you had told -- is that colleagues 10 that you've told that you're working on 11 the case? 12 A. I had explained why I wasn't 13 going to be here today. So -- and I had 14 to explain why I wasn't going to be 15 here -- why I went to the lawyers' 16 offices several times in the last couple 17 of weeks, so yes. 18 Q. Okay. Did you discuss any 19 details as far as your opinions -- 20 A. No. 21 Q. -- in the case? 22 Do you know Liz Swisher? 23 A. I don't know her personally. 24 I know her name, yes.</p>	<p style="text-align: right;">Page 93</p> <p>1 identification as Exhibit 2 Neel-6.) 3 BY DR. THOMPSON: 4 Q. Does this appear to be -- 5 this document appear to be invoices that 6 you've submitted? 7 A. Yes. 8 Q. And did you prepare these 9 invoices yourself? 10 A. Yes. 11 Q. And it looks to me that 12 you've worked on the case about 13 122 hours. Does that sound about right? 14 A. Probably. This doesn't even 15 include the latest invoice. So it's a 16 little bit more. Maybe 140 hours, 17 150 hours, something like that. 18 Q. And you're billing at \$750 19 an hour. 20 A. Yes. 21 Q. Correct? 22 What did you do to prepare 23 for your deposition today? 24 A. What did I do? I re-read</p>

<p style="text-align: right;">Page 94</p> <p>1 some of the papers. I read my report. I 2 read some of the expert reports. And I 3 had, as I just alluded to, several 4 discussions with Ms. Sharko and 5 Mr. Zellers. 6 Q. Did you meet -- when did you 7 meet with the attorneys? 8 A. I'd have to check my 9 calendar to get the exact dates. You 10 know, I have so many things to keep in my 11 head, I only try to retain the stuff 12 that's material. 13 Q. Has it been in the last few 14 days? 15 A. I met with them very briefly 16 yesterday. But yes, there have been a 17 couple of conferences. 18 Q. And for how long did you 19 meet yesterday? 20 A. An hour and a half maybe. 21 Maybe a little less. 22 Q. Let's go to your report now. 23 I didn't see a section of your report 24 that describes the methodology that you</p>	<p style="text-align: right;">Page 96</p> <p>1 that's trying to study the same issue 2 replicate what you did to formulate their 3 own opinions? 4 A. Well, the first thing they 5 could do is go to graduate school and 6 medical school, medical residency, 7 postdoctoral fellowship, and have 8 30 years in cancer biology. That would 9 be the background that you would need to 10 have my opinions in this report. 11 And assuming that you found 12 someone with that degree of training and 13 expertise, they would almost certainly do 14 exactly what I did. 15 Q. As you described reading the 16 references, searching for additional 17 references and then relying on your 39 -- 18 is it 39 years of experience? 19 A. I don't know. You'd have to 20 count it. It's very depressing for you 21 to keep repeating that number. 22 Q. That is the first time I've 23 repeated it. 24 A. That's the second time.</p>
<p style="text-align: right;">Page 95</p> <p>1 used to reach your opinions. Can you 2 describe for me as best you can how you 3 formulated the opinions that you gave in 4 your report? 5 A. I read references that are 6 listed in the report, consulted some 7 additional references that I found were 8 not material. I did the searches that I 9 explained earlier on GWAS.org and also on 10 the Sanger website and the CCLE website 11 at the Broad. 12 And I read the other expert 13 reports and some of their papers, and I 14 came up with my opinions. 15 Q. Can you refer me to a 16 published article or textbook chapter or 17 treatise or anything that actually 18 describes the methodology that you used 19 in formulating your opinions and writing 20 your report? 21 A. I don't think there is a 22 textbook that tells scientists how to 23 arrive at opinions. 24 Q. How would someone else</p>	<p style="text-align: right;">Page 97</p> <p>1 Q. Is it the second time? 2 Sorry about that. 3 A. I said it once, and that was 4 depressing enough. 5 Q. I'm afraid that I have more 6 experience -- or years than that. 7 But did you use the same 8 standards in reaching the opinions in 9 your report that you would use, for 10 example, if you were publishing a paper? 11 A. Yeah, I think that's 12 actually a good analogy. This is very 13 similar to a type of strategy that I 14 would use if I were writing a review 15 article. So I've written about 37 -- or 16 co-authored 37 review articles, or a book 17 chapter. That's the kind of approach 18 that I would use there. Very, very 19 similar. I should have said that 20 actually. That's a very good analogy. 21 Q. Oh, you're welcome. 22 Did you do a comprehensive 23 literature review on all relevant topics? 24 A. I did -- as I think I would</p>

<p style="text-align: right;">Page 98</p> <p>1 actually answer now the way you just 2 helped me answer, because I think that's 3 what -- I reviewed this to the degree of 4 depth that I would write an article on. 5 If I were going to write a review on 6 ovarian cancer and talc for a scientific 7 publication, this is the approach that I 8 would use.</p> <p>9 Q. Did you do any comprehensive 10 review on fibers and particles and their 11 role in carcinogenesis?</p> <p>12 A. No.</p> <p>13 Q. Did you do any literature 14 review on asbestos?</p> <p>15 A. Only a very limited amount 16 of review of asbestos in the context of 17 ovarian cancer.</p> <p>18 Q. Did you do any review on 19 fibrous talc?</p> <p>20 A. Not that I recall. Only in 21 the context of it might have been 22 mentioned in some of the papers that I 23 reviewed.</p> <p>24 Q. What is fibrous talc?</p>	<p style="text-align: right;">Page 100</p> <p>1 So I don't know how to 2 describe it any better than that. It's 3 very similar to the strict approach that 4 we would use for evaluating a new paper 5 we got to review.</p> <p>6 And that's the same standard 7 that I use when writing a review article. 8 I go to the literature, I read the papers 9 thoroughly, I don't take the conclusions 10 or the statements of the authors at face 11 value. I look to see whether the data 12 supports it -- whether the data support 13 it, and then I reach a conclusion, and 14 I -- I put that in the review in the 15 context of my evaluation of the paper. 16 And that's what I did here.</p> <p>17 Q. So as far as weighing the 18 evidence, would you agree that it's kind 19 of a gestalt, based on your education and 20 experience?</p> <p>21 MS. SHARKO: Object to the 22 form of the question.</p> <p>23 THE WITNESS: Can you define 24 gestalt? Because I know people</p>
<p style="text-align: right;">Page 99</p> <p>1 A. I can't describe. I'm not a 2 geologist. I'm a cancer biologist.</p> <p>3 Q. Did you use the particular 4 method to weigh the evidence from the 5 literature?</p> <p>6 A. I -- it's very hard -- you 7 know, it's very hard to describe how a 8 scientist evaluates data. We have a lot 9 of training in terms of looking at data 10 and assessing its strengths and 11 weaknesses and coming to a conclusion 12 about that.</p> <p>13 For example, I am an editor 14 of six -- I'm on the editorial board of 15 six major cancer journals. I review 16 papers all the time. I'm reviewing a 17 paper right now, for example, in one of 18 the other areas, not in ovarian cancer, 19 but one of the other areas that I 20 mentioned earlier. And I applied the 21 same standard to reviewing this 22 literature that I would apply to 23 reviewing a manuscript for Cell, Science, 24 Nature, all of these major journals.</p>	<p style="text-align: right;">Page 101</p> <p>1 use that in the common parlance. 2 And I want to make sure we're 3 being accurate, since it's on the 4 record and I'm testifying.</p> <p>5 BY DR. THOMPSON:</p> <p>6 Q. How would -- in the way that 7 you would define it.</p> <p>8 A. I think it's more like what 9 Potter Stewart said about pornography. 10 You know it when you see it, and I know 11 that the studies that I read on the 12 biological plausibility of talc are bad. 13 And I can state exactly why they're bad 14 in multiple ways. I think I did in my 15 report.</p> <p>16 Q. Yeah, and I'm sure you are 17 going to have more opportunity.</p> <p>18 But would you say it's more 19 subjective than objective?</p> <p>20 A. No, I would say it's quite 21 the contrary. It's quite objective. Bad 22 science is very objective. People who 23 are trained in the art can tell it.</p> <p>24 Q. But I'm talking about the</p>

<p style="text-align: right;">Page 102</p> <p>1 methodology, the objective methodology.</p> <p>2 A. I'm trying as best I can to</p> <p>3 explain the methodology.</p> <p>4 You read the paper, okay.</p> <p>5 You look at the data. You see if the</p> <p>6 data supports the claims. Okay. And</p> <p>7 unfortunately, in many journals, the data</p> <p>8 doesn't support the claims, even though</p> <p>9 the authors say it supports the claims.</p> <p>10 So, you know, there is a lot</p> <p>11 of papers that are published that either</p> <p>12 overstate their data or provide evidence</p> <p>13 that is not rigorous and they still get</p> <p>14 published, because, you know, there's a</p> <p>15 paper for every journal and a journal for</p> <p>16 every paper, as my mentor once said.</p> <p>17 Q. And that process is using</p> <p>18 your professional judgment I assume,</p> <p>19 right?</p> <p>20 A. I think judgment is a little</p> <p>21 soft there. It's using my professional</p> <p>22 experience.</p> <p>23 Q. Experience.</p> <p>24 A. And -- experience and</p>	<p style="text-align: right;">Page 104</p> <p>1 A. Absolutely.</p> <p>2 Q. Did you perform a Bradford</p> <p>3 Hill analysis to determine causation in</p> <p>4 this case?</p> <p>5 A. Well, I'm not an</p> <p>6 epidemiologist. Bradford Hill criteria</p> <p>7 are epidemiological criteria. I did, you</p> <p>8 know, read -- in the course of doing my</p> <p>9 research, I did read the Bradford Hill</p> <p>10 paper, and I did address several of the</p> <p>11 issues that Bradford Hill addressed.</p> <p>12 But, you know, as I said,</p> <p>13 my -- my expertise, as I think you know,</p> <p>14 is primarily in the area of cancer</p> <p>15 biology. And, you know, I did read the</p> <p>16 epidemiological literature from the</p> <p>17 standpoint of someone who is trained as a</p> <p>18 physician and also who is in charge of</p> <p>19 running the epidemiology and cancer</p> <p>20 control program for our cancer center</p> <p>21 grant. So I do have a little -- I have</p> <p>22 the ability to read that, but my</p> <p>23 expertise is primarily the cancer biology</p> <p>24 expertise. And that's where I -- I feel</p>
<p style="text-align: right;">Page 103</p> <p>1 judgment.</p> <p>2 Q. And judgment.</p> <p>3 A. Yes.</p> <p>4 Q. Okay.</p> <p>5 A. And training. I mean, you</p> <p>6 know, I've been doing this for a while.</p> <p>7 Q. 39 years, right?</p> <p>8 A. See, you're just doing that</p> <p>9 to upset me. It's not fair. It's not</p> <p>10 fair to upset the witness.</p> <p>11 Q. You know I'm going to get</p> <p>12 that in every time I can from now on.</p> <p>13 A. I'm going to have to</p> <p>14 calculate to see if it really is 39. It</p> <p>15 might be 38.</p> <p>16 Q. Regarding the report, do you</p> <p>17 intend to write up your opinions as to a</p> <p>18 review article in this case?</p> <p>19 A. I hadn't thought of doing</p> <p>20 it, no. But...</p> <p>21 Q. But you'd be willing to</p> <p>22 submit your report to -- for peer review?</p> <p>23 A. Sure.</p> <p>24 Q. Is that a fair assumption?</p>	<p style="text-align: right;">Page 105</p> <p>1 I have the most definitive training and</p> <p>2 expert and -- and knowledge.</p> <p>3 Q. So I think you'd agree that</p> <p>4 you are not an epidemiologist, per se?</p> <p>5 A. No, I'm not an</p> <p>6 epidemiologist. I think I stated that.</p> <p>7 Q. And -- and you don't hold</p> <p>8 yourself out to be an epidemiologist --</p> <p>9 A. No.</p> <p>10 Q. -- correct?</p> <p>11 Have you ever performed a</p> <p>12 Bradford Hill analysis in the course of</p> <p>13 your work as a cancer biologist?</p> <p>14 A. No.</p> <p>15 Q. Do you agree that scientists</p> <p>16 can look at the same body of literature</p> <p>17 and reach different conclusions?</p> <p>18 A. Sometimes.</p> <p>19 Q. And that's in a general</p> <p>20 sense, I'm asking that question.</p> <p>21 A. Sometimes. But not often.</p> <p>22 Q. So -- so credible and</p> <p>23 qualified scientists don't always agree.</p> <p>24 Would you say that's right?</p>

<p style="text-align: right;">Page 106</p> <p>1 A. When they don't agree, 2 that's because the data aren't strong 3 enough to reach agreement. The essence 4 of science is that it's empirical, which 5 means that people can make the same 6 observations in different places at 7 different times when using the same 8 methods. And they can, therefore, reach 9 the same conclusion. 10 When scientists disagree, 11 it's because the science is not settled. 12 Q. And you would agree that 13 there are often debates in medicine and 14 science? 15 A. I would answer the question 16 the same way I just answered. That when 17 there are debates in medicine and 18 science, it's because the science has not 19 established to a reasonable scientific 20 certainty that something is or isn't 21 true. 22 Q. And it's your opinion in 23 this case regarding the relationship 24 between the genital use of talcum powder</p>	<p style="text-align: right;">Page 108</p> <p>1 Q. You -- I just want to make 2 clear. 3 So in your opinion, the 4 science has settled that there's no 5 association, correct? 6 A. You -- you can't -- in 7 science you can't prove a negative. 8 So -- you can only prove a positive. And 9 I will restate my opinion, because that's 10 my opinion. 11 There is no credible 12 scientific evidence that perineal talc 13 causes ovarian cancer at all. There's no 14 evidence. 15 Q. Leave out the credible. Is 16 there no evidence? 17 A. In science there is no such 18 thing as unbelievable -- incredible 19 evidence. There's evidence and there's 20 bad science. 21 Q. Okay. 22 A. So if you'd like me to say 23 that there's bad science that claims that 24 ovarian cancer is caused by talc, I guess</p>
<p style="text-align: right;">Page 107</p> <p>1 and ovarian cancer, that the science is 2 settled? 3 A. No. It is my opinion that 4 there is no scientific evidence to 5 support the contention that talc applied 6 perineally causes ovarian cancer. There 7 is -- 8 Q. So the science is not 9 settled? 10 MS. SHARKO: Wait, wait. 11 Let him finish his answer. 12 DR. THOMPSON: You don't 13 have to remind me every time -- 14 when I do it, it's unintentional. 15 And I will pause as soon as I see 16 that he's going to continue to 17 talk. 18 BY DR. THOMPSON: 19 Q. Go ahead, Dr. Neel. 20 A. There is no -- the available 21 evidence does not support to any 22 scientific credibility that perineal talc 23 causes ovarian cancer. That is my 24 opinion.</p>	<p style="text-align: right;">Page 109</p> <p>1 I could say that. It's bad science. 2 Q. And I don't want you to say 3 anything. I just want -- want you to 4 give what your opinions are. 5 A. No, there is no credible -- 6 there is no credible scientific evidence 7 that perineal talc causes ovarian cancer 8 in my opinion. 9 DR. THOMPSON: I'm at a 10 breakpoint if that -- if this is a 11 good time for -- for you, Doctor? 12 THE WITNESS: Sure, I was 13 just going to say. I think that 14 would be good actually. 15 THE VIDEOGRAPHER: Remove 16 your microphone. The time is 17 10:21 a.m. Going off the record. 18 (Short break.) 19 THE VIDEOGRAPHER: We are 20 back on the record. The time is 21 10:40 a.m. 22 BY DR. THOMPSON: 23 Q. Dr. Neel, looking at your 24 report, Page 8, you have a section that</p>

<p style="text-align: right;">Page 110</p> <p>1 speaks of the hallmarks of cancer with a 2 reference to Dr. Hanahan's paper, 2011, 3 titled "Hallmarks of Cancer." And that's 4 just been marked as Exhibit 8. 5 (Document marked for 6 identification as Exhibit 7 Neel-8.) 8 BY DR. THOMPSON: 9 Q. You'll agree that this is a 10 classic paper in the field of cancer 11 biology, wouldn't you? 12 A. Yeah, it's a review article, 13 but yes. 14 Q. And -- right, a review 15 article. It does -- it's not reporting 16 primary research. 17 And reading in the abstract, 18 talking about the hallmarks of cancer 19 which include sustaining proliferative 20 signaling, evading growth suppressors, 21 resisting cell death, enabling 22 replicative immortality, inducing 23 angiogenesis, and activating invasion and 24 metastases.</p>	<p style="text-align: right;">Page 112</p> <p>1 A. Because the hallmarks are 2 the things you read. As it says, 3 underlying these hallmarks are certain 4 things. But the reason is that -- so 5 again, you have to distinguish between 6 inflammation that accompanies cancer and 7 those cancers that have a component of 8 inflammation in their initiation. I 9 think that's what we are talking about 10 here. 11 And there is no evidence 12 that ovarian cancer, or at least serous 13 cancers, which is the major topic here, 14 have inflammation as part of their, you 15 know, initiation phase. And there's 16 evidence against it. 17 Q. So it's your opinion that 18 inflammation does not play a role in the 19 initiation of ovarian cancer? 20 A. Yes. 21 Q. And you would -- 22 A. In high grade serous ovarian 23 cancer. 24 Q. And you would agree that</p>
<p style="text-align: right;">Page 111</p> <p>1 Did I read that correctly as 2 far as the hallmarks? 3 A. Yes. 4 Q. With some difficulty. 5 MS. SHARKO: Wait, wait. 6 Where are you reading from? 7 THE WITNESS: She's right 8 there. 9 MS. SHARKO: Oh, you are 10 reading from the paper. 11 THE WITNESS: Reading from 12 the text. 13 MS. SHARKO: Okay. 14 BY DR. THOMPSON: 15 Q. And then the next sentence, 16 "Underlying these hallmarks are genome 17 instability which generates the genetic 18 diversity that expedites their 19 acquisition, and inflammation, which 20 fosters multiple hallmark functions." 21 Why did you not mention 22 inflammation in your description of the 23 cancer hallmarks as reported by Hanahan 24 in his review article, 2011?</p>	<p style="text-align: right;">Page 113</p> <p>1 there are certainly other cancer 2 researchers that would disagree with that 3 opinion, correct? 4 A. I don't know who 5 specifically you're talking about. But I 6 would -- I'm happy to go over, you know, 7 whatever particular, you know, opinion 8 you are talking about. 9 Q. So you're not aware of any 10 scientist that would have the opinion 11 that inflammation can play a role in the 12 pathogenesis of epithelial ovarian 13 cancer? 14 A. No, I didn't say that. 15 MR. LOCKE: Objection to 16 form. 17 THE WITNESS: I didn't say 18 that. 19 There's clearly -- am I -- 20 MS. SHARKO: Answer. Go 21 ahead. 22 THE WITNESS: She's not 23 looking. So I assumed. 24 BY DR. THOMPSON:</p>

<p style="text-align: right;">Page 114</p> <p>1 Q. I just wanted to make sure I 2 asked the right question. And I think I 3 did, so --</p> <p>4 A. Okay. There's clearly 5 inflammation in ovarian cancer. But that 6 doesn't mean that inflammation is 7 involved in the initiation of ovarian 8 cancer, which is the issue under study 9 here. Okay.</p> <p>10 Q. And my question was about 11 the initiation.</p> <p>12 A. Okay. So in the context of 13 high grade serous cancer, there is no 14 compelling evidence that there is any 15 inflammation involved in that process. 16 If you look at -- we now know, and again 17 this is relatively recent information.</p> <p>18 But in the last 15 years or 19 so, it's becoming increasingly clear that 20 there are very well-defined 21 pre-neoplastic lesions on the fallopian 22 tube called STICs, which stands for 23 serous tubular intraepithelial 24 carcinomas -- and in serous tubal</p>	<p style="text-align: right;">Page 116</p> <p>1 which was not possible previously.</p> <p>2 DR. THOMPSON: Object as 3 nonresponsive.</p> <p>4 BY DR. THOMPSON:</p> <p>5 Q. Because my question was, are 6 there other scientists who would disagree 7 that inflammation does not play a role in 8 the pathogenesis of ovarian cancer?</p> <p>9 A. Well, again, in the -- I 10 don't think there's anybody who would 11 disagree with the statement that I just 12 made. Okay.</p> <p>13 I think that when -- there's 14 definitely inflammatory responses to the 15 cancer. Okay. And cancer does play -- 16 inflammation does play a role in the 17 pathogenesis of ovarian cancer from the 18 standpoint of when you have a fully 19 developed ovarian cancer, whether there's 20 inflammation present, and to what type of 21 inflammation will affect clinical 22 response and also survival.</p> <p>23 That doesn't mean that 24 inflammation is causal to ovarian cancer.</p>
<p style="text-align: right;">Page 115</p> <p>1 intraepithelial carcinomas -- and there's 2 earlier lesions that can be seen, called 3 STILs or p53 signatures.</p> <p>4 And those have been studied 5 pathologically by Malmberg, et al. and 6 also by, you know, Dr. Shi, whose 7 report -- expert report I did, has done 8 an independent -- I read, has done an 9 independent assessment.</p> <p>10 And if you look in those 11 lesions, there's no evidence of 12 inflammation. So that's -- we know for 13 sure that those lesions are 14 pre-neoplastic.</p> <p>15 So we have actually, since 16 the discovery of these lesions and the 17 underlying molecular pathogenesis that 18 accompanies these lesions, we're able to 19 say with quite a bit of scientific 20 confidence that they are pre-neoplastic 21 and in the case of STICs, the first stage 22 in ovarian cancer.</p> <p>23 So we actually can see 24 snapshots of the initiation process,</p>	<p style="text-align: right;">Page 117</p> <p>1 And I think that's where maybe there's 2 some confusion.</p> <p>3 Q. Would you agree that 4 carcinogenesis usually refers to, not 5 only the initiation, but the promotion 6 and progression of cancer?</p> <p>7 A. Yes. But I think that, 8 again, the cancer is present from the 9 standpoint once you have a STIC. So that 10 is a cancer.</p> <p>11 Q. So if there were scientists 12 that did believe that inflammation plays 13 a role in the pathogenesis of ovarian 14 cancer, not -- not limiting that to just 15 the initiation, would they just be wrong?</p> <p>16 A. I can't respond to a 17 hypothetical question like that without 18 seeing exactly what we're talking about. 19 So if you want to show me the actual 20 context of the statement, I'm happy to 21 offer an opinion one way or the other 22 about that. But I can't respond to a 23 sort of, with respect, somewhat vague 24 hypothetical about scientists of -- that</p>

<p style="text-align: right;">Page 118</p> <p>1 aren't specified and exactly what they 2 said.</p> <p>3 Q. How about other subtypes 4 besides serous?</p> <p>5 A. Yeah, again, the -- there 6 are data that, for example, pelvic 7 inflammatory disease may be involved in 8 some forms of low grade serous cancer. 9 But there it's not clear if it's the 10 inflammation or the agent itself. And 11 the recent data would suggest it's 12 probably a specific agent there as 13 opposed to inflammation, per se.</p> <p>14 Q. Back to the Hanahan article, 15 Page 658, "Emerging Hallmarks." And his 16 paper does not deal exclusively with 17 ovarian cancer. You'll agree, correct?</p> <p>18 A. Correct.</p> <p>19 Q. Under the chart, "Emerging 20 Hallmarks," he does list -- it's a he?</p> <p>21 A. Yeah. It's 22 Hanahan/Weinberg. I'm sure Bob Weinberg 23 would be very insulted if you thought 24 that he was --</p>	<p style="text-align: right;">Page 120</p> <p>1 cancer?</p> <p>2 MS. SHARKO: Object to the 3 form. Misstates his testimony.</p> <p>4 THE WITNESS: Yeah, again, 5 what I said before, was there's no 6 question that inflammatory cells 7 are involved in fully blown 8 ovarian cancer.</p> <p>9 If you look at a full -- if 10 I take an ovarian cancer from a 11 patient, it will have between 20 12 and sometimes up to 85 or 13 90 percent inflammatory cells.</p> <p>14 So there's no question that 15 the body tries to respond to the 16 cancer with an inflammatory 17 response. But that's not the same 18 as saying that inflammation is 19 involved in the pathogenesis of 20 ovarian cancer.</p> <p>21 For example, like 22 inflammation is clearly involved 23 in the pathogenesis of gastric 24 cancer caused by H. pylori.</p>
<p style="text-align: right;">Page 119</p> <p>1 Q. Yeah, I thought so. But 2 I -- a lot of our other papers are 3 written by women.</p> <p>4 And there is an emerging 5 hallmark described as tumor-promoting 6 inflammation. And you would agree that 7 tumor-promoting inflammation is an 8 emerging hallmark, correct?</p> <p>9 A. In certain cancers, 10 inflammation plays a very important rule. 11 There's no evidence that that's for 12 ovarian cancer. No compelling --</p> <p>13 Q. But you would agree that 14 other scientists have published that 15 inflammation does play a role in ovarian 16 cancer, correct?</p> <p>17 A. Again, I'm not sure what 18 exact publications that you're referring 19 to and in what context. So I can't 20 comment on a vague question like that. I 21 need to see the actual statement.</p> <p>22 Q. So you're not aware of any 23 literature where it is published that 24 inflammation plays a role in ovarian</p>	<p style="text-align: right;">Page 121</p> <p>1 So you have to -- you know, 2 you have to consider the 3 specifics, which is why I can't 4 comment on your, you know, 5 question about other scientists 6 and inflammation. I need to see 7 the actual claim.</p> <p>8 BY DR. THOMPSON:</p> <p>9 Q. Okay. Are the inflammatory 10 pathways outlined in the Hanahan study 11 plausible?</p> <p>12 A. Which inflammatory pathways 13 are you talking about?</p> <p>14 Q. The one that he describes --</p> <p>15 A. Where -- where are you in 16 the -- okay. So, for example, on page 17 664, immune inflammatory cells --</p> <p>18 I'm sorry. I lost my 19 microphone.</p> <p>20 Let's -- if you go to Page 21 664, under the title "Immune Inflammatory 22 Cells."</p> <p>23 "Also, as discussed above, 24 infiltrating cells of the immune system</p>

<p style="text-align: right;">Page 122</p> <p>1 are increasingly accepted to be generic 2 constituents of tumors." That's exactly 3 what I said. Okay. They are generic 4 constituents of tumors. That does not 5 speak to the initiation event. And again 6 these inflammatory cells operate in 7 conflicting ways, both tumor antagonizing 8 and tumor promoting -- 9 MS. SHARKO: You have to 10 read a little slower. 11 THE WITNESS: Oh, I'm sorry. 12 I switch into fast mode when I'm 13 reading. 14 MS. SHARKO: That's okay. 15 THE WITNESS: "These 16 inflammatory cells operate in 17 conflicting ways. Both 18 tumor-antagonizing and 19 tumor-promoting leukocytes can be 20 found in various proportions, if 21 not in most, all neoplastic 22 lesions." 23 So that's -- that's exactly 24 what I said before. The cancer --</p>	<p style="text-align: right;">Page 124</p> <p>1 A. No. Again, this was a 2 general -- 3 Q. That's a yes-no question. 4 You left that out of your report, right? 5 A. I didn't discuss it in 6 that -- in that particular place in my 7 report. 8 Q. Okay. Let's go to another 9 general cancer article. 10 You are familiar with 11 Dr. Balkwill I'm sure? 12 A. Yes. 13 Q. And Dr. Balkwill, I think, 14 was a featured speaker at one of your 15 conferences -- 16 A. I know Fran personally. 17 Q. -- and you know her. 18 A. Yes. 19 Q. Do you respect her as a 20 credible scientist? 21 A. Yes. 22 DR. THOMPSON: I'm going to 23 mark Dr. Balkwill's review 24 article.</p>
<p style="text-align: right;">Page 123</p> <p>1 there is no question that when you 2 have a cancer developing, that the 3 cell -- the body tries to respond 4 to it usually. And depending on 5 the nature of the response, that 6 response can antagonize the tumor 7 or it can help the tumor, because 8 the tumor adapts ways to respond 9 to it in a positive way. 10 BY DR. THOMPSON: 11 Q. And -- 12 A. But that's not initiation. 13 Q. Yeah, that wasn't my 14 question either. 15 A. Okay. 16 Q. But you will agree that in 17 using this review article to describe the 18 hall -- hallmarks of cancer, and it 19 wasn't a specific discussion of ovarian, 20 it was a discussion of all cancers, you 21 left out the -- several places in the 22 Hanahan report where the authors discuss 23 inflammation and its role in cancer, 24 correct?</p>	<p style="text-align: right;">Page 125</p> <p>1 (Document marked for 2 identification as Exhibit 3 Neel-9.) 4 MS. SHARKO: Do we have an 5 Exhibit 7? This is Exhibit 9, 6 right? 7 MR. ZELLERS: Yes, it should 8 be 9. The last one was 8. 9 (Whereupon, a discussion was 10 held off the record.) 11 DR. THOMPSON: I don't have 12 a 7 sticker. But we'll -- we'll 13 figure that out at the break. 14 BY DR. THOMPSON: 15 Q. Are you familiar with this 16 article -- 17 A. Yes. 18 Q. -- titled, "Inflammation and 19 cancer: Back to Virchow?" 20 A. Yes. Virchow. 21 Q. Virchow, sorry. 22 And this article, reading 23 from the abstract again, "Reviews the 24 links between cancer and inflammation and</p>

<p style="text-align: right;">Page 126</p> <p>1 discusses the implication of these links 2 for cancer prevention and treatment. We 3 suggest that the inflammatory cells and 4 cytokines found in tumors are more likely 5 to contribute to tumor growth, 6 progression, and immunosuppression than 7 they are to mount an effective host 8 anti-tumor response. Moreover cancer 9 susceptibility and severity may be 10 associated with functional polymorphisms 11 of inflammatory cytokine genes, and 12 deletion or inhibition of inflammatory 13 cytokines inhibits development of 14 experimental cancer. 15 "If genetic damage is the 16 'match that lights the fire' of cancer, 17 some types of inflammation may provide 18 the 'fuel that feeds the flames.'" 19 Would you agree with that 20 statement that Dr. Balkwill made in this 21 review article? 22 A. Which statement? There's a 23 number of statements there. 24 Would I agree with all of</p>	<p style="text-align: right;">Page 128</p> <p>1 inflammation and cancer risk. 2 Cancer risk would be the 3 cause or the initiation of cancer, right? 4 A. I'm not sure what she meant 5 there. But generally that's true. 6 Q. You wouldn't refer to risk 7 of -- when you have a cancer that's 8 already there, would you? 9 A. No, definitely not. 10 Q. And doctor -- 11 A. But actually in the -- can I 12 finish my statement? 13 But in the context of the 14 fact that cancer is a genetic disease and 15 the genetic damage that causes cancer is 16 what lights the fire, I think she's 17 actually said that this is not involved 18 in cancer initiation because this fuels 19 the flames. 20 So if you use her own 21 language, I think it supports my position 22 on this subject which has actually 23 developed much more since 2001. 24 Q. And I'm looking at</p>
<p style="text-align: right;">Page 127</p> <p>1 it? 2 Q. Would you agree with all of 3 that? 4 A. Insofar as it generally says 5 what's true in cancer in general, yes. 6 Insofar as it refers to specific issues 7 that are raised in my report and in my 8 testimony thus far, not completely. 9 And I would also note that 10 this paper is from 2001 which basically 11 makes it ancient history. 12 Q. And if you -- 13 A. Just so you -- can I just 14 complete that? 15 There's been more learned 16 about ovarian cancer in the last ten 17 years than in all of reported history 18 before then. So really, citing papers 19 from 2001 are really not relevant to 20 current ovarian cancer pathogenesis or 21 what our knowledge is of current ovarian 22 cancer pathogenesis. 23 Q. Looking at the chart, 24 Panel 1, some associations between</p>	<p style="text-align: right;">Page 129</p> <p>1 Panel 1 -- 2 A. Yes. 3 Q. -- some associations between 4 inflammation and cancer risk. 5 A. Mm-hmm. 6 Q. And it does list ovarian -- 7 A. Yes, it does. 8 Q. -- correct, in this chart? 9 A. Mm-hmm. 10 Q. And the inflammatory 11 stimulus or condition is listed as pelvic 12 inflammatory disease, talc, tissue 13 remodeling. 14 A. Mm-hmm. 15 Q. Is Dr. Balkwill wrong about 16 that? 17 A. Yes. She is incorrect 18 according to modern knowledge, yes, on 19 those details. 20 Q. Despite -- 21 A. The tissue remodeling is 22 probably correct. The other two are 23 unclear. More recent evidence does 24 suggest a possible connection with pelvic</p>

<p style="text-align: right;">Page 130</p> <p>1 inflammatory disease, as I already said. 2 But that's very -- very recent, hasn't 3 been firmly established yet. 4 And, in fact, the 5 conclusions of the articles that -- that 6 discuss the risk of pelvic inflammatory 7 disease state that more research is -- is 8 needed. 9 And I'm actually quite 10 interested in the recent abstract that 11 was at last year's ACR, I want to see if 12 the paper comes out on Chlamydia 13 trachomata and serous cancers, because 14 that would actually be quite interesting 15 as it would tie ovarian cancer 16 pathogenesis to a specific agent, which 17 has not been done before. 18 Q. And -- and -- 19 A. There is increasing evidence 20 that specific infectious agents are 21 actually relevant in various cancers. So 22 that would be interesting. 23 The talc data was quite 24 immature in 2001 so I don't really think</p>	<p style="text-align: right;">Page 132</p> <p>1 form. 2 THE WITNESS: So there's two 3 questions there. Can we break 4 them in half? 5 You said I've already 6 testified as to this. 7 What I testified to is that 8 I considered whatever was defined 9 as talc in the papers that I read. 10 And in some cases, specific talc 11 was defined as Johnson & Johnson 12 talc. 13 In others, it was just 14 generic talc. In still others it 15 was defined as, for example, talc 16 from Sigma. 17 We'd have to go through 18 every single paper to see what 19 talc was used in the particular 20 study. Some of the studies also 21 used a mixture -- not a mixture, 22 but they combined perineal powders 23 to include cornstarch. So each 24 paper is different, okay? We</p>
<p style="text-align: right;">Page 131</p> <p>1 it's even relevant to discuss it at this 2 point. I think that we've had many -- 3 much more data since then. And that the 4 same data was available to IARC in 2010 5 and they found it not, you know, 6 compelling. 7 Q. And IARC 2010 reviewing 8 literature up to 2006 specifically dealt 9 with non-asbestiform talc, correct? 10 A. The same talc that 11 Dr. Balkwill lists in this paper. 12 Q. How do you know what talc 13 she is referring to? 14 A. Well, she just says talc 15 which is, you know, basically -- if we 16 look at the paper I'm sure we can find 17 the citations to the same papers that 18 IARC considered. 19 Q. But you've -- you've already 20 testified that when you use talc, you're 21 referring to talcum powder products; 22 whereas, IARC was specific about 23 non-asbestiform talc, correct? 24 MR. LOCKE: Objection to</p>	<p style="text-align: right;">Page 133</p> <p>1 can't lump them together. 2 BY DR. THOMPSON: 3 Q. Okay. 4 A. What was the second half of 5 the question? Because I didn't catch 6 that. 7 Q. Let's go on. Have you 8 talked to Dr. Balkwill about the opinions 9 regarding talc in this paper? 10 A. No. As I told you, I 11 haven't spoken to anybody about my 12 opinions in this case. 13 Q. Did you review this paper 14 when you were looking at the subject of 15 talc and its relationship to ovarian 16 cancer? 17 A. I did scan through this 18 paper. That's -- I'm familiar with this 19 paper anyway. But as I said, it's from 20 2001. 2001 really is like, it's like 21 ancient history in cancer biology. I 22 know that sounds crazy, but it really is. 23 Q. You would agree that our 24 plaintiffs in this case, most of which</p>

<p style="text-align: right;">Page 134</p> <p>1 were using talcum powder throughout 2 decades, but certainly were using it in 3 2001, correct?</p> <p>4 A. I don't know what your -- I 5 don't know your specific plaintiffs, 6 except that I know that they had ovarian 7 cancer, for which I'm very sorry.</p> <p>8 Q. So when this paper came out 9 in 2001 stating that there was some 10 association between inflammation and 11 cancer risk, listing ovarian as the 12 malignancy that it applied to and talc as 13 an inflammatory stimulus and condition, 14 would that have caused anyone concern in 15 2001?</p> <p>16 MR. LOCKE: Objection.</p> <p>17 MS. SHARKO: Object to the 18 form.</p> <p>19 THE WITNESS: Who is 20 "anyone"?</p> <p>21 BY DR. THOMPSON:</p> <p>22 Q. Would that have caused you 23 concern about whether talc should be used 24 by women in the genital region in 2001</p>	<p style="text-align: right;">Page 136</p> <p>1 reviewed all of the literature in this 2 area.</p> <p>3 Q. I asked what she did.</p> <p>4 A. I don't know what she did.</p> <p>5 But we can look at her citations.</p> <p>6 Q. Have you spoken to 7 Dr. Balkwill about her opinions in this 8 paper?</p> <p>9 A. No. I said that I hadn't.</p> <p>10 Q. And when was the last time 11 that you spoke to her?</p> <p>12 A. The last time I saw Fran was 13 probably 2015, maybe. I don't know for 14 sure though. I saw her at a meeting.</p> <p>15 Q. Are you familiar with Simone 16 Reuter?</p> <p>17 A. Well, I don't know. I have 18 to see the spelling. Maybe I am and it's 19 just not pronounced correctly.</p> <p>20 (Document marked for 21 identification as Exhibit 22 Neel-10.)</p> <p>23 BY DR. THOMPSON:</p> <p>24 Q. And this is another review</p>
<p style="text-align: right;">Page 135</p> <p>1 when this paper was published?</p> <p>2 A. So -- okay, if I were 3 involved in regulation in 2001, I would 4 have done exactly what I did in this 5 case, which was to review the literature 6 available at the time. And I would have 7 found it wanting and not compelling, as 8 IARC did in 2010, when they reviewed the 9 literature that it was up to 2006, which 10 obviously included this paper in 2001.</p> <p>11 So I think that the fact 12 that it's stated in this paper as an 13 association, does not mean that 14 Dr. Balkwill did an extensive review of 15 the literature, as I did.</p> <p>16 And, therefore, I really 17 doubt that if Fran Balkwill were sitting 18 right here, she would say otherwise.</p> <p>19 Q. That's pure speculation, 20 correct?</p> <p>21 A. Okay. Yes.</p> <p>22 Q. You don't know what kind of 23 review she did?</p> <p>24 A. Well, I do know that I</p>	<p style="text-align: right;">Page 137</p> <p>1 article that will be Exhibit 10. Have 2 you seen this article before?</p> <p>3 A. I don't think so. But I 4 know these authors.</p> <p>5 Q. Okay. And are they credible 6 researchers scientists in your opinion?</p> <p>7 A. No.</p> <p>8 Q. And what led you to make 9 that conclusion?</p> <p>10 A. I've reviewed some papers by 11 the senior author and I find them to be 12 very poor.</p> <p>13 Q. These authors are at M.D. 14 Anderson Cancer Center in Houston, 15 correct?</p> <p>16 A. I don't know if they're 17 still there. But yes. This is --</p> <p>18 Q. That's where they wrote this 19 paper?</p> <p>20 A. -- from 2010.</p> <p>21 Q. And M.D. Anderson certainly 22 has a good reputation as a cancer center, 23 correct?</p> <p>24 A. Well, I actually</p>

1 participated in external reviews of
 2 various programs at M.D. Anderson. And I
 3 find some of the scientists are good and
 4 some of them are not very good. And I've
 5 written that, and knowing -- we
 6 participate in a review of one of the
 7 departments there. So I'm pretty
 8 familiar with the science at M.D.
 9 Anderson.

10 It's a gigantic institution,
 11 and the quality of the research varies
 12 from laboratory to laboratory.

13 Q. Okay. And this article is
 14 titled, from 2010, "Oxidative Stress,
 15 Inflammation, and Cancer: How Are They
 16 Linked?"

17 And in the abstract, the
 18 authors state, "How oxidative stress
 19 activates inflammatory pathways leading
 20 to transformation of a normal cell to
 21 tumor cell, tumor cell survival,
 22 proliferation, chemo resistance,
 23 radioresistance, invasion, angiogenesis,
 24 and stem cell survival is the focus of

1 this review."

2 Would you agree that those
 3 events, starting with inflammatory
 4 pathways leading to, are hallmarks of
 5 carcinogenesis?

6 A. I think that as I said
 7 before, in some cancers chronic
 8 inflammation is definitely part of the
 9 initiation event.

10 This paper is from 2010.
 11 And it is generically talking about
 12 pathways that are involved in cancer. It
 13 has no specific relevance to ovarian
 14 cancer. And in fact, as I said before,
 15 the evidence today in 2019, which is a
 16 lifetime ago from 2010 in cancer biology,
 17 directly assesses this with knowledge of
 18 the premalignant lesions and looking at
 19 the premalignant lesions and finding no
 20 inflammation.

21 Q. At what point in time can we
 22 consider an article that relates to
 23 ovarian cancer as relevant?

24 A. It depends on -- it depends

1 on the specific topic. Different things
 2 are developing at different times. So
 3 the genomics, for example, the genetic
 4 changes occurring, I would say largely
 5 defined in the beginning of 2012.

6 The evidence showing cell of
 7 origin is still somewhat emerging. It
 8 depends on the specific details.

9 Q. So any theory or any --
 10 scratch that.

11 Any mechanism that describes
 12 oxidative stress and inflammation as
 13 relevant to the pathogenesis of
 14 epithelial ovarian cancer is irrelevant?

15 A. No, I didn't say that.
 16 First of all, I think that you're
 17 conflating several things. Oxidative
 18 stress is separate from inflammation.
 19 They can be linked, they can be separate.
 20 We'd have to talk about each one of them
 21 separately.

22 In terms of oxidative
 23 stress, the oxidative stress in most
 24 cases that's associated with cancer

1 pathogenesis is coming from endogenous
 2 reactive oxygen formation that's
 3 catalyzed by cellular respiration through
 4 mitochondria and the uncoupling reactions
 5 that occur there.

6 Q. And any scientist who
 7 disagrees with that is wrong?

8 A. With what?

9 Q. What you just said?

10 A. Which part? That oxidative
 11 stress and inflammation are
 12 intellectually linked?

13 Q. That it's coming from --
 14 catalyzed by cellular rest through
 15 mitochondria --

16 A. Respiration.

17 Q. Respiration.

18 -- and not from exogenous or
 19 extrinsic factors.

20 A. It depends --

21 MS. SHARKO: Wait, wait.

22 What is the question?

23 BY DR. THOMPSON:

24 Q. That the cancer would be

<p style="text-align: right;">Page 142</p> <p>1 coming from mitochondrial respiration -- 2 endogenous mitochondrial respiration and 3 not extrinsic factors. 4 A. It depends on the specific 5 cancer and it depends on the specific 6 context. 7 For example, in the case of 8 H pylori induced gastric cancer, the 9 H pylori provokes inflammation, and the 10 inflammation results in the immigration 11 of immune cells and they may contribute 12 to oxidative stress by producing reactive 13 oxygen species. 14 But in many cancers, the 15 reactive oxygen is coming from endogenous 16 respiration, and one of the theories for 17 obesity and causing cancer goes through 18 that. 19 In the case of ovarian 20 cancer, there may be -- there is evidence 21 that is still emerging about whether 22 follicular fluid has reactive oxygen 23 species in it, and that may contribute to 24 the incessant ovulation hypothesis.</p>	<p style="text-align: right;">Page 144</p> <p>1 closely linked." 2 Do you agree or disagree 3 with that statement? 4 A. I agree with that for some 5 cancers, but I don't agree with that for 6 all cancers. 7 So, again, to talk about 8 cancer as an entity is even more 9 irrelevant than to talk about epithelial 10 ovarian cancer as a -- as an entity. 11 It's like talking about infectious 12 disease. 13 Q. Okay. And in Table 2 of 14 this article, the authors include a 15 partial list of cancers that have been 16 linked to reactive oxygen species. And 17 ovarian cancer is listed, isn't it? 18 A. We can look at the 19 reference. I have to see what the 20 reference is. 21 Q. Well, I'm just asking you if 22 it's listed in this table. 23 A. It's listed in the table. 24 Q. Okay. That was my question.</p>
<p style="text-align: right;">Page 143</p> <p>1 Q. Okay. I didn't ask about 2 H pylori or follicular fluid. 3 A. Well, you asked about 4 cancer. 5 MS. SHARKO: You don't need 6 to respond to that. She's going 7 to ask you another question. 8 BY DR. THOMPSON: 9 Q. These authors state, 10 "Overall, observations to date suggest 11 that oxidative stress, chronic 12 inflammation, and cancer are closely 13 linked." 14 Do you agree or disagree 15 with that statement? 16 A. I think that it depends on 17 the context and that that -- a general 18 statement like that is not necessarily 19 correct for any individual cancer. 20 Q. Well, the context is in a 21 review article about cancer in general. 22 "Overall, observations to 23 date suggest that oxidative stress, 24 chronic inflammation, and cancer are</p>	<p style="text-align: right;">Page 145</p> <p>1 In your report, you list the 2 differences between a risk factor and a 3 causal association, correct? 4 A. Yes. 5 Q. And what are those 6 differences? 7 A. A causal association has 8 some biological plausibility attached to 9 it, a mechanistic plausibility. 10 Q. And turning to Page 16 of 11 your report under plausibility. 12 MS. SHARKO: You can't write 13 on the exhibits. 14 THE WITNESS: Oh, I can't 15 draw? Sorry. 16 BY DR. THOMPSON: 17 Q. You state, "For an agent to 18 be adjudged the cause of cancer, there 19 must be a demonstration of a plausible 20 biochemical mechanism." 21 What do you mean by 22 demonstration? 23 A. What do I mean by 24 demonstration?</p>

<p style="text-align: right;">Page 146</p> <p>1 Q. Yes.</p> <p>2 A. Experiment, scientific, you</p> <p>3 know, proof. Evidence.</p> <p>4 Q. Doesn't that mean more than</p> <p>5 plausible?</p> <p>6 A. No.</p> <p>7 Q. Does plausible mean that</p> <p>8 there has to have been an experiment</p> <p>9 demonstrating the mechanism?</p> <p>10 A. There has to be some</p> <p>11 evidence that the mechanism is true, yes.</p> <p>12 You know, just a hypothesis is not</p> <p>13 plausibility. Not biochemical</p> <p>14 plausibility.</p> <p>15 Q. So in your opinion, the</p> <p>16 plausible mechanism has to be actually</p> <p>17 demonstrated by an experiment, correct?</p> <p>18 A. Yes.</p> <p>19 Q. Let's look at the Bradford</p> <p>20 Hill.</p> <p>21 I believe you used this</p> <p>22 reference when you were doing the</p> <p>23 Bradford Hill evaluation in your report?</p> <p>24 A. Which reference?</p>	<p style="text-align: right;">Page 148</p> <p>1 Bradford Hill, when originally providing</p> <p>2 his guidelines, did not require that the</p> <p>3 mechanism be demonstrated by</p> <p>4 experimentation?</p> <p>5 MS. SHARKO: Well, you</p> <p>6 didn't read that whole -- the</p> <p>7 whole section. Right?</p> <p>8 DR. THOMPSON: I read what I</p> <p>9 read.</p> <p>10 If Dr. Neel needs to read</p> <p>11 the whole section to answer my</p> <p>12 question, he can.</p> <p>13 THE WITNESS: Yeah. This</p> <p>14 was in the context -- I read the</p> <p>15 whole paper. And this was in the</p> <p>16 context of when you have a hazard</p> <p>17 ratio of like, 240 to 1, like they</p> <p>18 did for chimney sweeps, then, you</p> <p>19 know, the requirement for</p> <p>20 experiment is less.</p> <p>21 But for, you know, a series</p> <p>22 of epidemiological associations</p> <p>23 which are conflicting and weak,</p> <p>24 the biological plausibility</p>
<p style="text-align: right;">Page 147</p> <p>1 Q. The Bradford Hill 1965. The</p> <p>2 original report.</p> <p>3 A. Mm-hmm.</p> <p>4 DR. THOMPSON: And I'll go</p> <p>5 ahead and mark this Exhibit 11.</p> <p>6 (Document marked for</p> <p>7 identification as Exhibit</p> <p>8 Neel-11.)</p> <p>9 BY DR. THOMPSON:</p> <p>10 Q. Let's actually look at --</p> <p>11 this will be Page 4, Page 298 of the</p> <p>12 original paper.</p> <p>13 A. Page 2. Line what?</p> <p>14 Q. 298, under plausibility.</p> <p>15 A. Yep.</p> <p>16 Q. And at least the Bradford</p> <p>17 Hill framework under plausibility states,</p> <p>18 "It will be helpful if the causation we</p> <p>19 suspect is biologically plausible. But</p> <p>20 this is a feature I am convinced we</p> <p>21 cannot demand. What is biologically</p> <p>22 plausible depends on the biological</p> <p>23 knowledge of the day."</p> <p>24 Would you agree with me that</p>	<p style="text-align: right;">Page 149</p> <p>1 becomes essential.</p> <p>2 And then also this paper was</p> <p>3 written in 1965 when cancer</p> <p>4 biology was developed to a far</p> <p>5 lesser extent.</p> <p>6 So I think that the general</p> <p>7 standard for a cancer biologist to</p> <p>8 accept causation would require</p> <p>9 experiments in 2019. And I state</p> <p>10 that as an editor -- a member of</p> <p>11 the editorial board of six</p> <p>12 journals, including the two most</p> <p>13 prominent cancer biology journals.</p> <p>14 I can assure you that no one</p> <p>15 would accept a manuscript for</p> <p>16 publication in a high quality</p> <p>17 journal that did not have evidence</p> <p>18 of biological plausibility</p> <p>19 supported by experiments in 2019.</p> <p>20 BY DR. THOMPSON:</p> <p>21 Q. I'm just asking you</p> <p>22 Dr. Hill's statements regarding</p> <p>23 plausibility.</p> <p>24 A. Well, I suspect Dr. Hill is</p>

<p style="text-align: right;">Page 150</p> <p>1 no longer alive, but this is from 1965. 2 And I don't think we should be applying 3 1965 standards to 2019 science. 4 Q. Isn't that what you applied 5 in your report when you did the causation 6 analysis? 7 A. I applied the general 8 frame -- I applied the general framework. 9 I didn't apply the -- every conclusion in 10 Dr. Hill's paper. 11 Q. Okay. 12 A. Standards change over time. 13 Q. But looking at Bradford 14 Hill, as published in 1965, and as you 15 said, you applied in your report to some 16 degree, you would agree that the 17 mechanism does not have to be proven, 18 correct? 19 A. The mechanism does not have 20 to be proven to say what? 21 Q. To say that -- to be 22 causative, the mechanism for how the 23 agent is associated with an outcome, that 24 causative, that it doesn't have to be</p>	<p style="text-align: right;">Page 152</p> <p>1 think you can find a credible scientist 2 in the world -- or in the United States 3 or the world who would say otherwise. 4 That is generally accepted scientific 5 practice in 2019. 6 Q. And that's Dr. Neel's 7 standard? 8 A. No. That is generally 9 accepted scientific practice in 2019. 10 I'm sure that if -- you 11 know, if you asked any other significant 12 scientist in the United States, they 13 would agree with that statement. 14 Q. But where can I find that 15 published? 16 A. I don't -- I mean I don't 17 know if it is published. But that is 18 generally the -- that is definitely the 19 standard. 20 Q. You would agree that 21 plausible and demonstrable do not mean 22 the same thing, right? 23 A. In the context of biological 24 plausibility, yes, they do -- they do</p>
<p style="text-align: right;">Page 151</p> <p>1 proven? 2 A. There has to be some 3 evidence for it. Some -- some credible 4 scientific evidence for which there is 5 none in the current case. 6 Q. Where could I find the -- 7 the standard that you apply that it has 8 to be demonstrated in an experiment for 9 something to be causal? 10 A. Where could you find that 11 standard? 12 Q. Where would I find an 13 article that says that's the standard 14 that should be used? 15 A. I'm telling you, I'm telling 16 you as a scientist who is the editor of 17 major scientific journals and a reviewer 18 for every major scientific journal, that 19 that is the accepted standard in science. 20 If you ask any major 21 scientist in the United States what is 22 the accepted standard for establishing 23 causation, they will tell you a 24 mechanism-based experiment. I don't</p>	<p style="text-align: right;">Page 153</p> <p>1 mean the same thing essentially. 2 They mean experimentally 3 demonstrated or experimentally supported. 4 Q. Does the Bradford Hill 5 analysis require the evidence to be 6 compelling? 7 A. I don't know what -- what 8 the Bradford Hill analysis means, whether 9 Bradford Hill -- it doesn't mean -- I 10 don't know if he uses the word 11 compelling. We can read through the 12 entire thing. 13 Again, I want to clarify, I 14 used the Bradford Hill framework to reach 15 my conclusions. I didn't necessarily use 16 every single statement in Bradford Hill's 17 paper. 18 Q. I agree. But I'm just 19 talking about the Bradford Hill 20 guidelines that you cited and applied in 21 your report. 22 A. Framework. 23 Q. Do -- does the Bradford Hill 24 framework require that the evidence be</p>

<p style="text-align: right;">Page 154</p> <p>1 compelling?</p> <p>2 A. We can read through the</p> <p>3 whole thing and see if he uses the word</p> <p>4 "compelling."</p> <p>5 Q. Okay. Go ahead.</p> <p>6 A. Okay.</p> <p>7 Q. It would be under biological</p> <p>8 plausibility. That's what we're</p> <p>9 referring to.</p> <p>10 A. Well, again, as I said</p> <p>11 before, the -- this is one of the</p> <p>12 criteria. If the other criteria are</p> <p>13 weak, this becomes extremely important.</p> <p>14 And there is no strong evidence of</p> <p>15 anything else.</p> <p>16 So I don't really -- I don't</p> <p>17 know if he uses the word "compelling" in</p> <p>18 here. But in my opinion, in order to</p> <p>19 establish biological plausibility, there</p> <p>20 has to be compelling scientific evidence,</p> <p>21 yes.</p> <p>22 Q. Okay. All right. In your</p> <p>23 opinion, does a Bradford Hill analysis</p> <p>24 require the evidence to be convincing?</p>	<p style="text-align: right;">Page 156</p> <p>1 used the Bradford Hill analysis, as a</p> <p>2 framework.</p> <p>3 Q. And direct and plausible</p> <p>4 mean different things, right?</p> <p>5 A. Direct and plausible mean</p> <p>6 different things? They clearly mean</p> <p>7 different things, but they don't mean</p> <p>8 different things in the context of</p> <p>9 convincing scientific evidence of</p> <p>10 biological plausibility.</p> <p>11 Q. Okay. So in --</p> <p>12 A. The common use --</p> <p>13 Q. In the way that you have</p> <p>14 interpreted a causation analysis, a</p> <p>15 plausible mechanism would need to be</p> <p>16 direct evidence, correct?</p> <p>17 MS. SHARKO: Were you done</p> <p>18 with your last answer?</p> <p>19 THE WITNESS: I can answer</p> <p>20 it in the context of this</p> <p>21 question.</p> <p>22 Can you repeat the question</p> <p>23 though?</p> <p>24 BY DR. THOMPSON:</p>
<p style="text-align: right;">Page 155</p> <p>1 A. Yes. Not a Bradford Hill.</p> <p>2 My analysis. I can't really comment on</p> <p>3 what Bradford Hill would see as the</p> <p>4 standard.</p> <p>5 As I said, I used the</p> <p>6 Bradford Hill framework to frame my</p> <p>7 report. I did not use Bradford Hill's</p> <p>8 personal opinion, obviously. I used my</p> <p>9 scientific opinion.</p> <p>10 Q. Okay. But I'm -- but you</p> <p>11 had referred to the Bradford Hill</p> <p>12 analysis in your report, so I'm just</p> <p>13 trying to understand how you used that</p> <p>14 analysis in --</p> <p>15 A. As a framework.</p> <p>16 Q. -- as a framework.</p> <p>17 Did the Bradford Hill</p> <p>18 analysis require that evidence be direct?</p> <p>19 A. As I said, I used the</p> <p>20 Bradford Hill -- the Bradford Hill paper</p> <p>21 as a framework to discuss the issues</p> <p>22 regarding the pathogenesis of ovarian</p> <p>23 cancer and the relationship, if any, to</p> <p>24 talc. Okay. That is the only way that I</p>	<p style="text-align: right;">Page 157</p> <p>1 Q. In the way that you have</p> <p>2 interpreted a causation analysis, a</p> <p>3 plausible mechanism would need to be</p> <p>4 direct evidence, correct?</p> <p>5 A. It would need to be direct</p> <p>6 experimental evidence.</p> <p>7 Q. Direct experimental</p> <p>8 evidence.</p> <p>9 A. Yes, yes.</p> <p>10 Q. And --</p> <p>11 A. And can I finish? I</p> <p>12 actually wasn't finished.</p> <p>13 Q. I'm sorry.</p> <p>14 A. Direct experimental evidence</p> <p>15 that is scientifically credible that</p> <p>16 there is a causal relationship between</p> <p>17 the agent and the disorder under</p> <p>18 question, whether it's neoplastic or not.</p> <p>19 Q. And same thing with</p> <p>20 definitive. Does the Bradford Hill</p> <p>21 framework work require that for evidence</p> <p>22 to be plausible, it should be definitive?</p> <p>23 A. Again, I'm not using -- I'm</p> <p>24 using Bradford Hill criteria as a</p>

<p style="text-align: right;">Page 158</p> <p>1 framework for addressing the issues of 2 causation here in my report. 3 I don't know whether -- 4 whether -- what was -- what was the word? 5 Credible? 6 Q. We're on definitive. 7 A. Definitive. In my 8 professional opinion, evidence has to be 9 definitive to attribute causation. Yes. 10 And by definitive, I mean 11 credible scientific data to support the 12 plausibility claim. And there is none in 13 this case. 14 Q. Does the evidence under a 15 Bradford Hill framework for the mechanism 16 to be plausible need to be conclusive? 17 A. Again, I'm going to say the 18 same thing that I said before. 19 In order to have an argument 20 in favor of biological plausibility, the 21 data has to be conclusive and convincing. 22 Bad data are of no use. Bad 23 experiments are of no use. Sometimes 24 they are of less than no use, because</p>	<p style="text-align: right;">Page 160</p> <p>1 not a risk factor for epithelial ovarian 2 cancer? 3 A. That states it's not? 4 Q. Yes. An article that says 5 we have reviewed the evidence and talcum 6 powder is not a risk factor for 7 epithelial -- 8 A. I think that it's not an 9 established risk factor. There is no -- 10 there is no agreement on talc being a 11 risk factor for ovarian cancer. So it's 12 not an established risk factor. 13 I think, you know, we can go 14 to my report, but I'm pretty sure 15 statements were made to that effect by 16 IARC, possible. They said the data 17 aren't compelling. So yes. 18 Q. Is it not what -- is it that 19 it's not well established, or is it not a 20 risk factor? 21 A. There is no compelling 22 evidence. There is no credible 23 scientific evidence that it's a risk 24 factor. There is no consistent evidence</p>
<p style="text-align: right;">Page 159</p> <p>1 they are misleading. 2 Q. And this is the last one. 3 A. Sure. 4 Q. And I just want to 5 understand words that you have used in 6 your report. 7 A. Mm-hmm. 8 Q. Using a Bradford Hill 9 framework, does evidence for plausibility 10 need to be strong? 11 A. In my opinion, to attribute 12 causation of any agent to the initiation 13 of any malignancy, the evidence has to be 14 strong, convincing, and definitive, yes. 15 Q. Okay. Let's move on to 16 another topic. 17 Is it your opinion that the 18 genital use of talcum powder is not a 19 risk factor for epithelial ovarian 20 cancer? 21 A. Yes. That's my opinion. 22 Q. And can you cite any 23 literature that explicitly states that 24 talcum powder use in the perineal area is</p>	<p style="text-align: right;">Page 161</p> <p>1 that it's a risk factor. There is no 2 agreed-upon definition that it's a risk 3 factor. 4 Q. Is it a possible risk 5 factor? 6 A. I think that, you know, IARC 7 considers it a possible carcinogen as of 8 2010. 9 I think the evidence that's 10 developed 2010 makes it less likely that 11 it's even possible. 12 Q. Could credible scientists 13 look at the evidence and determine that 14 the genital use of talcum powder is a 15 risk factor for ovarian cancer? 16 A. No, not in my opinion. I 17 don't think so. 18 Q. So would those doctors or 19 scientists, looking at the evidence and 20 reaching those opinions be uninformed? 21 A. I can't comment on the basis 22 of their opinions without seeing their 23 opinions. 24 Q. But at least in your</p>

<p style="text-align: right;">Page 162</p> <p>1 opinion, they could not credibly come to 2 that conclusion?</p> <p>3 A. Not based on the evidence 4 that I reviewed and considered in my 5 report, no.</p> <p>6 Q. Okay. And you have a 7 section in your report on risk factors 8 for ovarian cancer in which you discuss 9 some of them, beginning on Page 12.</p> <p>10 You only cite one article, 11 and that is the Reid paper. And we'll 12 mark that as 12.</p> <p>13 (Document marked for 14 identification as Exhibit 15 Neel-12.)</p> <p>16 MS. SHARKO: Where -- where 17 are you talking about?</p> <p>18 THE WITNESS: It's on the 19 next page.</p> <p>20 MS. SHARKO: So we're not on 21 Page 12.</p> <p>22 DR. THOMPSON: Well, it 23 begins multiple factors likely 24 contribute to ovarian cancer, on</p>	<p style="text-align: right;">Page 164</p> <p>1 Do they state that?</p> <p>2 A. Actually I think you're 3 misstating their conclusions. I'll read 4 their conclusions.</p> <p>5 Q. Well, I -- only --</p> <p>6 A. "However a" --</p> <p>7 Q. I --</p> <p>8 A. You asked me a question. 9 Can I answer it?</p> <p>10 Q. I -- I am reading, did I 11 read this correctly: "Other possible 12 risk factors include environmental and 13 lifestyle factors such as asbestos and 14 talc powder exposures and cigarette 15 smoking."</p> <p>16 Did I read that correctly?</p> <p>17 A. Where are you reading at?</p> <p>18 Q. In the abstract?</p> <p>19 MS. SHARKO: So wait a 20 minute. You asked him a question. 21 He tried to answer it. You 22 interrupted him.</p> <p>23 DR. THOMPSON: Well, I asked 24 him --</p>
<p style="text-align: right;">Page 163</p> <p>1 Page 12.</p> <p>2 THE WITNESS: I got it.</p> <p>3 BY DR. THOMPSON:</p> <p>4 Q. This is the paper that you 5 refer to in your report as really the 6 only paper that you -- that you cite on 7 risk factors for ovarian cancer, correct?</p> <p>8 A. Yes, because it's the most 9 recent comprehensive review on the 10 subject.</p> <p>11 Q. And the authors are 12 epidemiologists, correct?</p> <p>13 A. Yes.</p> <p>14 Q. They are not physicians, 15 correct?</p> <p>16 A. No, but Tom Sellers is an 17 expert in ovarian cancer epidemiology. I 18 know him personally. He is the director 19 of Moffitt Cancer Center in Tampa.</p> <p>20 Q. And the authors actually 21 state that "other possible risk factors 22 include environmental and lifestyle 23 factors such as asbestos and talc powder 24 exposures."</p>	<p style="text-align: right;">Page 165</p> <p>1 MS. SHARKO: He gets to 2 answer the question or you 3 withdraw it.</p> <p>4 DR. THOMPSON: I asked him 5 if they stated that. He did not 6 need to tell me about something 7 else when I was asking the 8 question, was that stated by the 9 authors.</p> <p>10 MS. SHARKO: You don't need 11 to raise your voice. He's trying 12 to answer your question.</p> <p>13 DR. THOMPSON: Okay. All 14 right.</p> <p>15 Let's just start all over. 16 I think the record will speak for 17 itself.</p> <p>18 BY DR. THOMPSON:</p> <p>19 Q. Dr. Neel, do the authors 20 state --</p> <p>21 A. Where are you quoting from 22 first?</p> <p>23 Q. In the abstract, the next to 24 the last sentence.</p>

<p style="text-align: right;">Page 166</p> <p>1 Do the authors state:</p> <p>2 "Other possible risk factors include</p> <p>3 environmental and lifestyle factors such</p> <p>4 as asbestos and talc powder exposures and</p> <p>5 cigarette smoking"?</p> <p>6 A. Yes, that's what it says</p> <p>7 there. But it's out -- you are reading</p> <p>8 it out of context.</p> <p>9 Q. I just ask if they say that.</p> <p>10 But you didn't include in</p> <p>11 your report where you use this article,</p> <p>12 that the authors stated that possible</p> <p>13 risk factors include environmental and</p> <p>14 lifestyle factors such as asbestos and</p> <p>15 talc exposure, did you?</p> <p>16 A. The entire -- my entire</p> <p>17 report was focused around talc. The</p> <p>18 other -- what I cited in this context, in</p> <p>19 my report, were the other claimed risk</p> <p>20 factors in ovarian cancer. I was</p> <p>21 discussing the other risk factors. The</p> <p>22 rest of the report concerns my views on</p> <p>23 talc as a risk factor. So there was no</p> <p>24 reason to cite it here. The entire</p>	<p style="text-align: right;">Page 168</p> <p>1 So I -- I don't really think</p> <p>2 there's any conflict here.</p> <p>3 And you stated out of</p> <p>4 context what's in the abstract.</p> <p>5 And -- and again, a lot of</p> <p>6 times when authors are setting up</p> <p>7 a paper, they will post, you know,</p> <p>8 all possibilities that are in the</p> <p>9 literature and then they will</p> <p>10 reach their own conclusions.</p> <p>11 So for you to lift that out</p> <p>12 of context is really not accurate</p> <p>13 in my opinion.</p> <p>14 BY DR. THOMPSON:</p> <p>15 Q. And did you review any other</p> <p>16 articles that discussed risk factors for</p> <p>17 ovarian cancer other than the Reid paper?</p> <p>18 A. Yes, I -- I read multiple</p> <p>19 papers on ovarian cancer pathogenesis,</p> <p>20 but I can't tell you right now.</p> <p>21 I cited this one, because</p> <p>22 this is the most up-to-date comprehensive</p> <p>23 view of ovarian cancer risk factors.</p> <p>24 And my goal in my report was</p>
<p style="text-align: right;">Page 167</p> <p>1 report concerns that.</p> <p>2 But again, I must insist</p> <p>3 that you are taking out of context</p> <p>4 Dr. Reid -- Dr. Sellers' conclusions. I</p> <p>5 found Dr. Sellers' conclusions to be</p> <p>6 quite consistent with my own based on the</p> <p>7 actual section --</p> <p>8 Q. And you'll have another</p> <p>9 opportunity if Ms. Sharko wants to come</p> <p>10 back.</p> <p>11 MS. SHARKO: Wait.</p> <p>12 Were you done with your</p> <p>13 answer?</p> <p>14 THE WITNESS: I was almost</p> <p>15 done. Okay.</p> <p>16 MS. SHARKO: Finish your</p> <p>17 answer.</p> <p>18 THE WITNESS: If one goes to</p> <p>19 Page 18 of the same paper that</p> <p>20 you're citing, and actually reads</p> <p>21 the section on asbestos and talcum</p> <p>22 powder, you will see that his</p> <p>23 opinions and mine are almost</p> <p>24 identical.</p>	<p style="text-align: right;">Page 169</p> <p>1 not to write a review of all the risk</p> <p>2 factors for ovarian cancer. The goal of</p> <p>3 my report and the topic which I'm here to</p> <p>4 testify here today on, is the role of</p> <p>5 talc and Johnson & Johnson products in --</p> <p>6 and the possible role of talc and Johnson</p> <p>7 & Johnson products in ovarian cancer</p> <p>8 pathogenesis.</p> <p>9 The entirety of my report</p> <p>10 focuses primarily on that issue. This</p> <p>11 section on other risk factors was in the</p> <p>12 context of background of other issues</p> <p>13 concerning ovarian cancer. Not whether</p> <p>14 or not talc was involved.</p> <p>15 Q. Okay. Let's just look at</p> <p>16 some other articles relating to risk</p> <p>17 factors --</p> <p>18 A. Sure.</p> <p>19 Q. -- and see if there are</p> <p>20 scientists that disagree with that</p> <p>21 opinion.</p> <p>22 A. Well, I just want to clarify</p> <p>23 again. Dr. Sellers does not --</p> <p>24 MS. SHARKO: Wait, wait,</p>

<p style="text-align: right;">Page 170</p> <p>1 wait.</p> <p>2 THE WITNESS: -- disagree</p> <p>3 with my opinion.</p> <p>4 BY DR. THOMPSON:</p> <p>5 Q. I -- we have moved on from</p> <p>6 Dr. Sellers.</p> <p>7 A. Okay. Well, you said other</p> <p>8 scientists so I just want to get --</p> <p>9 Q. Well, I'm about to show</p> <p>10 you --</p> <p>11 A. Okay.</p> <p>12 MS. SHARKO: She's going to</p> <p>13 ask you a new question.</p> <p>14 BY DR. THOMPSON:</p> <p>15 Q. I'm going to ask you a new</p> <p>16 question.</p> <p>17 MS. SHARKO: That was just a</p> <p>18 speech.</p> <p>19 THE WITNESS: Okay.</p> <p>20 MS. SHARKO: Wait for a</p> <p>21 question.</p> <p>22 THE WITNESS: I thought that</p> <p>23 was -- okay.</p> <p>24 MS. SHARKO: Okay.</p>	<p style="text-align: right;">Page 172</p> <p>1 these authors.</p> <p>2 Q. Okay. That wasn't the</p> <p>3 question.</p> <p>4 Under lifestyle factors,</p> <p>5 these authors state, "A lot of work has</p> <p>6 been done to clarify the risk reduction</p> <p>7 of various lifestyle approaches, such as</p> <p>8 alcohol, obesity, cigarette smoking and</p> <p>9 talc use. Some of these are subtype</p> <p>10 specific, such as endometriosis,</p> <p>11 cigarette smoking and obesity, while</p> <p>12 others are general risk factors.</p> <p>13 "Use of talc in the genital</p> <p>14 area has consistently been shown to</p> <p>15 increase the risk of ovarian cancer and,</p> <p>16 therefore, is not recommended."</p> <p>17 Did I read that correctly?</p> <p>18 A. Yes, you did.</p> <p>19 Q. So these authors at least do</p> <p>20 consider talc use a risk factor, correct?</p> <p>21 A. Apparently.</p> <p>22 Q. And -- and consider it a</p> <p>23 general risk factor, even understanding</p> <p>24 that there are some risk factors that are</p>
<p style="text-align: right;">Page 171</p> <p>1 There is exhibit -- what is</p> <p>2 that, 13?</p> <p>3 (Document marked for</p> <p>4 identification as Exhibit</p> <p>5 Neel-13.)</p> <p>6 BY DR. THOMPSON:</p> <p>7 Q. And I'm handing you</p> <p>8 Exhibit 13, which comes from a textbook</p> <p>9 titled "Cancer Prevention and Screening."</p> <p>10 And if you will turn to</p> <p>11 Page 337.</p> <p>12 MS. SHARKO: Do you have the</p> <p>13 year on this?</p> <p>14 THE WITNESS: 2019. It's on</p> <p>15 the bottom of the first page.</p> <p>16 BY DR. THOMPSON:</p> <p>17 Q. So you would agree that --</p> <p>18 A. What page please?</p> <p>19 Q. 337.</p> <p>20 A. Okay.</p> <p>21 Q. So you'll agree that this is</p> <p>22 an up-to-date chapter in a textbook as</p> <p>23 well?</p> <p>24 A. Yes, but I've never heard of</p>	<p style="text-align: right;">Page 173</p> <p>1 subtype specific, correct?</p> <p>2 A. Well, I think these authors</p> <p>3 have no knowledge of modern cancer</p> <p>4 biology, because it's not possible to</p> <p>5 cause the same genetic defects with a</p> <p>6 different agent that works by different</p> <p>7 mechanisms.</p> <p>8 Q. So the authors of this paper</p> <p>9 in your opinion are wrong?</p> <p>10 A. Yes, in my opinion.</p> <p>11 I should also -- can I just</p> <p>12 say one other thing about this?</p> <p>13 Q. Yes.</p> <p>14 A. It's notable that they cite</p> <p>15 references for alcohol, obesity and</p> <p>16 cigarette smoking, but they don't cite</p> <p>17 any references for talc use. So I can't</p> <p>18 respond to --</p> <p>19 Q. And there's no -- there's no</p> <p>20 question pending on the table.</p> <p>21 MS. SHARKO: Let him finish.</p> <p>22 Let him finish.</p> <p>23 MS. O'DELL: There's no</p> <p>24 question --</p>

<p style="text-align: right;">Page 174</p> <p>1 DR. THOMPSON: There's no 2 question. 3 THE WITNESS: I didn't 4 finish my answer. 5 MS. O'DELL: This is not his 6 opportunity just to speak without 7 a question. There is no question. 8 MS. SHARKO: He was 9 answering the question. 10 DR. THOMPSON: He was not 11 answering my question. 12 MS. SHARKO: That's your 13 opinion, because you don't like 14 it. Dr. Neel, finish your answer. 15 BY DR. THOMPSON: 16 Q. Exhibit -- Exhibit 14 -- 17 MS. SHARKO: Stop. Dr. 18 Neel, finish your answer. 19 BY DR. THOMPSON: 20 Q. Are you finished with your 21 question, Dr. Neel? 22 A. No, I was saying -- 23 Q. I mean your answer. 24 A. -- in reading the piece --</p>	<p style="text-align: right;">Page 176</p> <p>1 risk factors, but I didn't cite one 2 article about talc, which is the issue. 3 Q. Dr. Neel, if you would try 4 as best you can to answer my question. 5 A. I am answering your 6 question. 7 Q. And my question was just did 8 you cite one article. And the answer 9 would be yes. 10 I just handed you a paper -- 11 MR. LOCKE: Objection. 12 MS. SHARKO: You don't -- 13 you don't need to respond to that 14 speech. Let's move on to the next 15 exhibit. 16 DR. THOMPSON: I don't think 17 I had a question. 18 (Document marked for 19 identification as Exhibit 20 Neel-14.) 21 BY DR. THOMPSON: 22 Q. The next article is from 23 2012, "Ovarian Cancer Etiology, Risk 24 Factors, and Epidemiology."</p>
<p style="text-align: right;">Page 175</p> <p>1 the part that you mentioned, it's notable 2 that they don't reference anything for 3 their statement on talc use. It would be 4 much more helpful if we could see what 5 evidence they want to adduce to make 6 their claim. 7 I provided very substantial 8 evidence in support of my opinions. And 9 I've also been able to discuss them. 10 This is, you know, an 11 isolated statement if a textbook that, 12 you know, probably hasn't undergone 13 scientific review. 14 Q. Well, risk factors, you 15 cited one article. We'll make that 16 clear. 17 MS. SHARKO: Well, wait. 18 No, wait a minute. You don't just 19 get to lob out comments. 20 BY DR. THOMPSON: 21 Q. Did you cite one article in 22 your risk factor discussion in your 23 paper? 24 A. I cited one article about</p>	<p style="text-align: right;">Page 177</p> <p>1 And these authors, turning 2 to Page 6, have a chart listing risk 3 factors for epithelial ovarian cancer. 4 If you'll turn to that, it's 5 on Page 6. 6 A. Yeah I have it. 7 MS. SHARKO: And this is 8 Exhibit 14 for the record. 9 DR. THOMPSON: Exhibit 14. 10 MS. SHARKO: Thank you. 11 BY DR. THOMPSON: 12 Q. And at least these authors, 13 list under inflammatory risk factors that 14 increase the risk for ovarian cancer, 15 perineal talc use, endometriosis, and 16 pelvic inflammatory disease. 17 Would you agree that these 18 authors list talc -- perineal talc 19 exposure as a risk factor? 20 A. They do. But this is 21 completely non-consummate with modern 22 research. 23 Q. I'm just asking you if the 24 authors list it.</p>

<p style="text-align: right;">Page 178</p> <p>1 A. Yes, they --</p> <p>2 Q. Okay. And so these</p> <p>3 scientists who do feel -- are of the</p> <p>4 opinion that it's a risk factor are</p> <p>5 wrong?</p> <p>6 A. I don't know that they're</p> <p>7 scientists. I mean, they --</p> <p>8 Q. They're doctors. These</p> <p>9 doctors --</p> <p>10 A. There's a big difference</p> <p>11 between a doctor and a scientist. Since</p> <p>12 I have both degrees, I can state that to</p> <p>13 a very strong degree of confidence.</p> <p>14 Q. Are you saying that someone</p> <p>15 has to have two degrees to --</p> <p>16 A. No, but I'm saying that I'm</p> <p>17 very familiar with the difference in the</p> <p>18 training of the average physician and the</p> <p>19 average scientist and their ability to</p> <p>20 evaluate scientific data, and they're not</p> <p>21 the same.</p> <p>22 Q. The next one --</p> <p>23 A. There are definitely --</p> <p>24 Can I finish? There are</p>	<p style="text-align: right;">Page 180</p> <p>1 to any particular agent's ability to</p> <p>2 cause any kind of cancer.</p> <p>3 We know a lot -- and by the</p> <p>4 way, again, you're citing papers from</p> <p>5 2012. That's a lifetime ago in cancer</p> <p>6 biology, and specifically in ovarian</p> <p>7 cancer pathogenesis. We know much more</p> <p>8 about the cell and molecular biology of</p> <p>9 ovarian cancer today than we did then.</p> <p>10 And the fact that they put</p> <p>11 endometriosis in here is exemplary of</p> <p>12 that, because we know that endometriosis</p> <p>13 is a risk factor only insofar as the</p> <p>14 cancer is probably coming from the</p> <p>15 endometrial cells.</p> <p>16 Q. And let's turn --</p> <p>17 A. It's a cell of origin issue.</p> <p>18 It's not a carcinogenesis issue.</p> <p>19 Q. The next -- the next paper</p> <p>20 that I'm going to give you is titled</p> <p>21 "Risk Factors For Ovarian Carcinoma."</p> <p>22 (Document marked for</p> <p>23 identification as Exhibit</p> <p>24 Neel-15.)</p>
<p style="text-align: right;">Page 179</p> <p>1 definitely physicians who are eminently</p> <p>2 qualified to evaluate scientific data.</p> <p>3 But the average practicing physician is</p> <p>4 not able to evaluate modern molecular</p> <p>5 data like the molecular biologist or</p> <p>6 cancer biologist. They're different</p> <p>7 disciplines.</p> <p>8 Q. If an M.D., gynecologic</p> <p>9 oncologist, who is familiar with the</p> <p>10 literature in the field gives an opinion</p> <p>11 that talcum powder use in the genital</p> <p>12 area can cause or contribute to ovarian</p> <p>13 cancer, are they wrong?</p> <p>14 A. Possibly. In my opinion</p> <p>15 they're wrong, because I've reviewed the</p> <p>16 literature comprehensively including the</p> <p>17 molecular literature, which they are</p> <p>18 probably not capable of evaluating, and</p> <p>19 they're not capable -- the average</p> <p>20 gynecologist oncologist is definitely not</p> <p>21 capable of evaluating the modern</p> <p>22 molecular data, such as mutational</p> <p>23 signatures and other more modern and</p> <p>24 comprehensive analyses that would speak</p>	<p style="text-align: right;">Page 181</p> <p>1 BY DR. THOMPSON:</p> <p>2 Q. And this was published in</p> <p>3 2018, correct?</p> <p>4 A. Mm-hmm.</p> <p>5 Q. If you'll turn to Page 4.</p> <p>6 MS. SHARKO: So for the</p> <p>7 record, this is Exhibit 15.</p> <p>8 DR. THOMPSON: I'm sorry.</p> <p>9 Exhibit 15.</p> <p>10 MS. SHARKO: Okay. Thank</p> <p>11 you.</p> <p>12 DR. THOMPSON: I'll try to</p> <p>13 be better about that.</p> <p>14 BY DR. THOMPSON:</p> <p>15 Q. This article titled "Risk</p> <p>16 Factors For Ovarian Cancer," if you'll</p> <p>17 turn to Page 4. There's a chart with</p> <p>18 risk factors.</p> <p>19 And this particular paper</p> <p>20 does divide the risk factors up by</p> <p>21 subtype, correct?</p> <p>22 A. Yes.</p> <p>23 MS. SHARKO: You are allowed</p> <p>24 to read the paper.</p>

<p style="text-align: right;">Page 182</p> <p>1 THE WITNESS: I'm looking at 2 it, yeah. 3 MS. SHARKO: Okay. 4 THE WITNESS: Mm-hmm. 5 BY DR. THOMPSON: 6 Q. And the heading for Table 1 7 is "Summary of Putative Cells of Origin 8 and Identified Risk Factors For Specific 9 Ovarian Cancer Histologic Subtypes," 10 correct? 11 A. Yes. 12 Q. And so these authors at 13 least considered the different subtypes 14 when they were trying to classify the 15 risk factors, correct? 16 A. Yes. 17 Q. And if you'll look in this 18 chart under the heading Lifestyle Risk 19 Factors, "Genital powder use is included 20 under subtype all serous and subtype 21 endometrioid and subtype clear cell." 22 A. Mm-hmm. 23 Q. Do you agree that authors 24 considered that a risk factor for those</p>	<p style="text-align: right;">Page 184</p> <p>1 Looking at the -- and it was 2 published in 2018? 3 A. Mm-hmm. 4 Q. Looking at the end of the 5 paper, page -- I don't see the page. But 6 at the very end before, in -- in 7 summary -- 8 A. In the discussion? 9 Q. In -- in discussion, 10 conclusions. It states, "In particular, 11 talc powder use" -- 12 A. I'm sorry, I can't see where 13 we are. 14 Q. They -- 15 A. Oh, I see. Okay. I got it. 16 Q. In the last -- next to the 17 last paragraph. 18 "In particular, talc powder 19 use is highly prevalent in the African 20 American community and has been found to 21 be associated with increased risk of 22 ovarian cancer in this and other studies. 23 Indeed, regression models excluding talc 24 use overestimated the associations in our</p>
<p style="text-align: right;">Page 183</p> <p>1 three subtypes? 2 A. Yes. 3 Q. Are these authors wrong? 4 A. Yes. And the reason they 5 are wrong is because, if you look at the 6 mutational signature, the type of 7 molecular causation of clear cell and 8 endometrioid cancer, it's completely 9 different than the molecular basis for 10 serous ovarian cancer. 11 One of them is caused by 12 chromosome abnormalities in copy number 13 variations, and the other is caused by 14 point mutations in pathways that I've 15 spent my entire career studying. 16 (Document marked for 17 identification as Exhibit 18 Neel-16.) 19 BY DR. THOMPSON: 20 Q. Next, Exhibit 16. 21 This is another paper that 22 discusses risk factors. It's part of the 23 African American cancer epidemiology 24 study that's published numerous articles.</p>	<p style="text-align: right;">Page 185</p> <p>1 analysis." 2 Do you agree that these 3 authors consider talc use to result in 4 increased risk of ovarian cancer in 5 African American population? 6 A. This is yet another of many 7 case-control studies which, you know, 8 claim to see an association. But they 9 are subject to the same type of recall 10 bias and other classification bias that 11 is prone to be found in case-control 12 studies. 13 The cohort studies don't 14 show this. And they are much more 15 reliable in my opinion. 16 That -- you know, so yes, 17 they say it, but that doesn't make it 18 true. 19 Q. So these authors are wrong 20 to consider talc use a risk factor for 21 ovarian cancer? 22 A. I don't think they've done a 23 complete analysis of the literature and 24 they are probably not capable of</p>

<p style="text-align: right;">Page 186</p> <p>1 evaluating the molecular issues. 2 (Document marked for 3 identification as Exhibit 4 Neel-17.) 5 BY DR. THOMPSON: 6 Q. The next article is marked 7 Exhibit 17. It's a patient by Wu and her 8 colleagues. 9 MS. SHARKO: It's a paper. 10 DR. THOMPSON: What did I 11 say? 12 MS. SHARKO: Patient. 13 DR. THOMPSON: Sorry. Oh 14 boy. 15 BY DR. THOMPSON: 16 Q. It's a paper. 17 MS. SHARKO: It's almost 18 like a patient. 19 BY DR. THOMPSON: 20 Q. Let's -- let's ask that 21 question over again. 22 Exhibit 17 is a paper by 23 Dr. Wu that discusses the nongenetic risk 24 factors for ovarian cancer, correct?</p>	<p style="text-align: right;">Page 188</p> <p>1 to be a confirmed nongenetic risk factor 2 for ovarian cancer? 3 A. They apparently do. 4 Q. And are these authors wrong 5 as well? 6 A. Yes. And I -- I -- 7 Q. You didn't hesitate with 8 that opinion, did you? 9 A. No. Because again, if 10 you -- if you -- you're pulling out 11 individual case-control studies. And we 12 already know that 60 percent of the 13 case-control -- 67 percent of the 14 case-control studies reach one 15 conclusion, 33 percent reach the other 16 conclusion, and all the cohort studies 17 are negative. 18 That is why if you read a 19 review like Dr. Sellers' review, which is 20 a comprehensive review of the recent 21 literature concerning risk factors, you 22 will find an opinion very similar to 23 mine, which is that there is no 24 compelling evidence that talc was a</p>
<p style="text-align: right;">Page 187</p> <p>1 A. Mm-hmm. 2 Q. And under the discussion 3 section of this paper, the authors state 4 that, first paragraph, "With the high 5 mortality" -- 6 A. Where -- I'm sorry, I have 7 to find it. 8 Q. Under discussion, first 9 paragraph. Page 1098. 10 "With the high mortality and 11 the lack of effective early screening for 12 ovarian cancer, better understanding of 13 preventive risk factors is a priority. 14 The primary motivation for this analysis 15 was to determine whether the six 16 confirmed nongenetic risk factors for 17 IEOC (parity, use of oral contraceptives, 18 tubal ligation, endometriosis, first 19 degree family history of ovarian cancer, 20 and use of genital talc in non-Hispanic 21 whites are also risk factors in Hispanics 22 and African Americans)." 23 Do you agree that these 24 authors believe the use of genital talc</p>	<p style="text-align: right;">Page 189</p> <p>1 causal -- is a cause of ovarian cancer. 2 And that's the basis of my opinion. 3 This is an -- this is a 4 single paper of a case-control study and, 5 you know, that's not as strong as 6 considering the entire body of the 7 evidence as I've done in my report. 8 Q. But doctors and scientists 9 that have a different opinion as you've 10 stated are wrong, correct? 11 MS. SHARKO: Object to the 12 form of the question. 13 THE WITNESS: In -- in each 14 individual case, I'm happy to tell 15 you whether I think they are wrong 16 or not. Okay. 17 Since I haven't met every 18 doctor and scientist who may have 19 a particular opinion, it would be 20 inappropriate for me to say that 21 all doctors and scientists who 22 have a different opinion are 23 wrong. 24 If someone comes up with</p>

Page 190

1 some evidence that is convincing,
 2 I will change my opinion. Right
 3 now, all of the available evidence
 4 suggests that there is no
 5 association between genital talc
 6 and ovarian cancer. And some of
 7 their evidence says that there
 8 isn't.

9 So there is no evidence to
 10 support the case that genital talc
 11 application causes ovarian cancer
 12 in my scientific opinion.

13 BY DR. THOMPSON:

14 Q. Where is the evidence that
 15 there isn't?

16 A. Where is the evidence that
 17 there isn't?

18 Q. I think I asked you that
 19 before and you could not cite to an
 20 article that said it is not a risk
 21 factor.

22 A. I --

23 Q. So I would like for you to,
 24 if you do have one, I would like to know

Page 191

1 what --

2 A. Oh. So --

3 MS. SHARKO: Object. Object
 4 to the form of the question.
 5 Lacks foundation. Misstates his
 6 testimony and apparently asked and
 7 answered since you said you asked
 8 it before.

9 DR. THOMPSON: Well, he had
 10 a different answer. I wanted to
 11 clarify it.

12 MS. SHARKO: I don't think
 13 so.

14 BY DR. THOMPSON:

15 Q. Dr. -- Dr. Neel, do you
 16 have -- just so I am clear.
 17 Do you have an article that
 18 you can point to that explicitly states
 19 that talcum powder is not a risk factor
 20 for ovarian cancer?

21 A. So that was a different
 22 question than you just asked before.
 23 The -- the question you asked before is
 24 do I have a paper that says that genital

Page 192

1 talc is not a risk factor for ovarian
 2 cancer. And I said that was a risk
 3 factor question.

4 If you ask me is there any
 5 evidence that genital talc causes ovarian
 6 cancer, there are several papers which
 7 argue against that and I'm happy to cite
 8 those.

9 Q. My question was risk
 10 factors, so...

11 A. Okay. But you didn't ask
 12 that question right before. So I was
 13 answering it -- you know, you changed
 14 your question, which is why it's a
 15 different answer.

16 If you ask me the second
 17 question I'd be happy to tell you.

18 Q. Okay. So just to be clear,
 19 the answer to the question is, is there a
 20 paper that explicitly states that talcum
 21 powder is not a risk factor of ovarian
 22 cancer, you don't have one to point to?

23 A. There are -- there are many
 24 papers that review the literature --

Page 193

1 Q. I need a yes or no --

2 A. You misstate --

3 Q. -- question.

4 MS. SHARKO: No, no, no.
 5 Wait. Timeout.

6 THE WITNESS: You asked --

7 DR. THOMPSON: Well, he is
 8 answering all kinds of questions
 9 that are not what I'm asking.

10 MS. SHARKO: Well, I
 11 disagree. But you've asked your
 12 question. He's entitled to answer
 13 it. If you want to withdraw your
 14 question so be it.

15 But you can't interrupt him
 16 because you don't --

17 DR. THOMPSON: No, I want an
 18 answer to my question.

19 MS. SHARKO: -- you don't
 20 like his answer.

21 DR. THOMPSON: Okay. Let's
 22 go back and see what the question
 23 and answer were.

24 BY DR. THOMPSON:

Page 194

1 Q. Just to be clear, is there a
2 paper that explicitly states that talcum
3 powder is not a risk factor of ovarian
4 cancer? You don't have one to point to.

5 And his answer, is there are
6 many papers --

7 A. You didn't let me finish.
8 Would you like me to finish?

9 Q. Okay. Well, the question
10 though was point me to a paper that
11 explicitly states that talcum powder is
12 not a risk factor for ovarian cancer.

13 A. Scientists don't generally
14 speak in that language. What they would
15 say is very similar to what Dr. Sellers
16 said, and which most of the review
17 articles about this topic say and what I
18 say. Which is there is no credible
19 scientific evidence that.

20 That is how scientists
21 speak. We have a language that we use,
22 just like lawyers have a language that
23 lawyers use.

24 And in scientific credence

Page 195

1 saying that -- in scientific language,
2 saying that there's no credible
3 scientific evidence is the way we would
4 state the -- the conclusion. And that's
5 how I'm stating it. That's very similar
6 to how Dr. Sellers concluded it. And
7 I -- I think that's the essence of my
8 statement.

9 Q. So your answer would be
10 you're not able to answer that question?

11 MR. LOCKE: Objection.

12 THE WITNESS: No, my answer
13 is exactly what I said.

14 BY DR. THOMPSON:

15 Q. Okay. We'll -- we'll move
16 on.

17 But I don't believe I got
18 the answer to the question: Can you
19 point me to an article that states that
20 talcum powder is not a risk factor for
21 ovarian cancer?

22 MS. SHARKO: All right.

23 That's not a question. That's an
24 editorial comment.

Page 196

1 BY DR. THOMPSON:

2 Q. Can you point me --

3 MS. SHARKO: No. You asked
4 him that question already.

5 DR. THOMPSON: But I still
6 haven't got an answer. I'm going
7 to try one more time.

8 BY DR. THOMPSON:

9 Q. Can you point me to an
10 article that explicitly states that
11 talcum powder is not a risk factor for
12 ovarian cancer?

13 MS. SHARKO: Objection.
14 Asked and answered.

15 You may not like the answer,
16 but you got an answer.

17 DR. THOMPSON: Okay. The
18 record will speak for itself that
19 there is not an answer.

20 MS. O'DELL: It was asked
21 but never answered. He didn't
22 answer the question.

23 MS. SHARKO: Okay. I
24 thought -- I thought your side

Page 197

1 said the rule was that only one
2 lawyer can talk.

3 MS. O'DELL: I think the
4 evidence will show, the record
5 will show over depositions that
6 you weren't defending, Susan, you
7 had plenty to say, so I don't know
8 that I would raise that.

9 DR. THOMPSON: Including
10 last week.

11 MS. SHARKO: So the rules
12 are that one lawyer gets to
13 question the witness. So let's --

14 MS. O'DELL: I'm not
15 questioning the witness. But I'm
16 free to speak and I will speak.

17 MS. SHARKO: You know what?
18 It seems like maybe we should just
19 take a lunch break and let
20 everybody simmer down.

21 DR. THOMPSON: I only
22 have -- I don't need a lunch
23 break.

24 MR. TISI: I'm going to tell

<p style="text-align: right;">Page 198</p> <p>1 you, can I have that section?</p> <p>2 MS. SHARKO: So now we have</p> <p>3 a third plaintiff's lawyer</p> <p>4 talking?</p> <p>5 MR. TISI: No, no, no.</p> <p>6 We're off -- we're not talking</p> <p>7 about this.</p> <p>8 Can I have that clipped,</p> <p>9 Ms. Sharko's comment so I can use</p> <p>10 it in other depositions going</p> <p>11 forward? Please, thank you. You</p> <p>12 can send me that.</p> <p>13 Because I expect we're going</p> <p>14 to need it going forward, given</p> <p>15 her behavior in the past.</p> <p>16 Thank you.</p> <p>17 DR. THOMPSON: Okay.</p> <p>18 MS. SHARKO: You know,</p> <p>19 Mr. Tisi, behave yourself.</p> <p>20 DR. THOMPSON: I want -- I</p> <p>21 want to move on.</p> <p>22 MR. TISI: I -- I don't need</p> <p>23 to be schooled by you.</p> <p>24 BY DR. THOMPSON:</p>	<p style="text-align: right;">Page 200</p> <p>1 unclear.</p> <p>2 Q. What -- how do you define a</p> <p>3 carcinogen?</p> <p>4 A. A carcinogen? A carcinogen</p> <p>5 is an agent that causes cancer.</p> <p>6 Q. And that would include</p> <p>7 initiation?</p> <p>8 A. Mm-hmm.</p> <p>9 Q. And promotion?</p> <p>10 A. Probably -- so there's a</p> <p>11 difference between health scientists and</p> <p>12 experimental carcinogenecist would define</p> <p>13 a carcinogen and how the public would use</p> <p>14 the word carcinogen.</p> <p>15 In the common parlance, a</p> <p>16 promotor, a tumor promoter would probably</p> <p>17 be considered a carcinogen. But in</p> <p>18 scientific language a carcinogen is just</p> <p>19 the initiating event.</p> <p>20 Q. But you'll agree that in</p> <p>21 some context at least, scientists refer</p> <p>22 to a carcinogen in each of those phases?</p> <p>23 A. Yes. Mm-hmm, yes.</p> <p>24 Q. And is it -- is that</p>
<p style="text-align: right;">Page 199</p> <p>1 Q. Is it -- is it your</p> <p>2 opinion --</p> <p>3 MS. SHARKO: Yeah, because</p> <p>4 you don't listen.</p> <p>5 MR. TISI: That's because --</p> <p>6 that's because I wouldn't listen</p> <p>7 to somebody who tries to school</p> <p>8 me.</p> <p>9 DR. THOMPSON: I really</p> <p>10 don't want to waste my time, so...</p> <p>11 BY DR. THOMPSON:</p> <p>12 Q. Is it your -- Dr. Neel, is</p> <p>13 it your opinion that asbestos is not a</p> <p>14 risk factor for ovarian cancer?</p> <p>15 A. I don't have an opinion on</p> <p>16 asbestos in ovarian cancer. I haven't</p> <p>17 really given enough study to --</p> <p>18 Q. Okay. So you don't have an</p> <p>19 opinion one way or the other as to</p> <p>20 whether asbestos --</p> <p>21 A. Not -- not a strong opinion,</p> <p>22 no.</p> <p>23 Q. Okay. Any opinion?</p> <p>24 A. I think the evidence is</p>	<p style="text-align: right;">Page 201</p> <p>1 sometimes referred to as a complete</p> <p>2 carcinogen?</p> <p>3 A. That's a kind of old term,</p> <p>4 but yes.</p> <p>5 Q. I'm old.</p> <p>6 MS. SHARKO: Do you want</p> <p>7 that on the record?</p> <p>8 DR. THOMPSON: What the hey.</p> <p>9 MS. SHARKO: You are not</p> <p>10 old, Margaret.</p> <p>11 DR. THOMPSON: Thank you,</p> <p>12 Susan. That's the nicest thing</p> <p>13 you've said today.</p> <p>14 MS. SHARKO: Chris will</p> <p>15 order that page too.</p> <p>16 MR. TISI: I was -- I was</p> <p>17 going to say. I was going to -- I</p> <p>18 wouldn't qualify it by today. I'd</p> <p>19 make it a year, but go ahead.</p> <p>20 BY DR. THOMPSON:</p> <p>21 Q. So let's go to Page 14 of</p> <p>22 your report --</p> <p>23 A. Do you have a long question?</p> <p>24 Because if not, I'm going to have to take</p>

<p style="text-align: right;">Page 202</p> <p>1 a break. That coffee is having its 2 effect. 3 Q. I'm fine breaking for lunch 4 or -- 5 A. If it's a short question I 6 can answer it. 7 MS. SHARKO: No, we don't 8 want -- 9 THE WITNESS: Okay. 10 DR. THOMPSON: Yeah, 11 let's -- let's go -- this is 12 actually a natural break so... 13 THE WITNESS: Okay. 14 MS. SHARKO: Okay. 15 THE VIDEOGRAPHER: Stand by, 16 please. The time is 11:54 a.m. 17 Off the record. 18 - - - 19 (Lunch break.) 20 - - - 21 THE VIDEOGRAPHER: We are 22 back on the record. The time is 23 1:02 p.m. 24 BY DR. THOMPSON:</p>	<p style="text-align: right;">Page 204</p> <p>1 transformation of ovarian cancer cells or 2 that talc causes inflammation that's 3 relevant to ovarian cancer pathogenesis. 4 Q. So just to shorten that a 5 little bit, there's no credible evidence 6 that there's a plausible biological 7 mechanism for any association between -- 8 A. Yes. 9 Q. Let me finish, sir. 10 A. Sorry. 11 Q. -- between -- just so the 12 record is clear -- 13 A. Sorry. 14 Q. -- between talcum powder use 15 and ovarian cancer? 16 A. Yes. That's my testimony. 17 Q. So this morning we discussed 18 risk factors, cause, association. This 19 afternoon I'd like to delve into that 20 molecular cellular mechanism a little bit 21 more if that's okay. 22 On Page 12 of your report, 23 next to the last paragraph, you state, 24 "Taken together these findings clearly</p>
<p style="text-align: right;">Page 203</p> <p>1 Q. Dr. Neel, this morning you 2 testified that you are not an 3 epidemiologist. 4 Is it fair to say that your 5 opinions in this case are focused on 6 whether or not there's credible evidence 7 that talcum powder can cause ovarian 8 cancer from a molecular standpoint? 9 A. I would say from a molecular 10 and -- and cellular standpoint. 11 Q. From a molecular and 12 cellular standpoint? 13 A. Yes. 14 Q. And it's your opinion that 15 there's no cause and effect. But is it 16 also your opinion that there's no 17 plausible biological mechanism for any 18 association between talcum powder use and 19 ovarian cancer? 20 A. I don't think there's any 21 evidence one way or the -- any credible 22 evidence one way or the other. 23 So there's no -- there's no 24 credible evidence that talc causes</p>	<p style="text-align: right;">Page 205</p> <p>1 show that different types of ovarian 2 cancer originate in different cell types 3 that suffer different types of mutations 4 which are unlikely to be caused by the 5 same environmental agent." 6 Explain that sentence to me. 7 A. Okay. So there is Type 1 8 tumors and there's Type 2 tumors, and the 9 Type 1 tumors are caused largely by point 10 mutations, and the Type 2 tumors are 11 caused largely by copy number 12 abnormalities or copy number variation 13 and rearrangements. And the underlying 14 mutagenic mechanisms that cause point 15 mutations and the repair defects that 16 cause point mutations are distinct from 17 the types of mutations -- mutational 18 processes that cause copy number 19 variation and translocations. 20 So an agent that does one 21 kind of genetic event is not likely to 22 cause the other. 23 Q. Do you have -- what is the 24 basis for that opinion? In other words,</p>

<p style="text-align: right;">Page 206</p> <p>1 what article could you direct me to that 2 would make that same claim? 3 A. I can't cite an article 4 off -- that's general scientific 5 knowledge in my field. I can't cite a 6 specific article. 7 Q. So it's not possible in your 8 opinion that the same environmental agent 9 could cause the molecular changes in both 10 types of cancers or more than one type of 11 cancer? 12 A. It's -- I think I said it's 13 unlikely. 14 Q. Oh, unlikely. So -- 15 A. That's the word I'd like to 16 stick with, unlikely. 17 Q. -- stick with unlikely. 18 Okay. 19 A. I didn't say possible. I 20 said unlikely. 21 Q. Okay. And I wasn't trying, 22 in that case, to -- to trick you. I 23 was -- I was just trying to understand -- 24 A. Did you want to just tell me</p>	<p style="text-align: right;">Page 208</p> <p>1 and in some cases whole genome 2 sequencing, has so many different types 3 of mutations that you can actually 4 categorize the mutations according to 5 their carcinogenic agent. 6 So benzopyrenes have a 7 particular mutational signature. And so 8 you can actually see which forms of lung 9 cancer are caused by that signature and 10 which forms aren't. 11 So for example, nonsmokers 12 can get lung cancer, but smokers are 13 about 20 to 25 times more likely to get 14 cancer, and the cancers that come from 15 smoking have a characteristic molecular 16 signature, whereas the cancers that come 17 from -- that come in nonsmokers do not 18 have the character -- do not have the 19 same signature. So you can tell them 20 apart easily. 21 Q. And even different types of 22 cancer that are caused by smoking have 23 the -- that same molecular signature? 24 A. No, not all signature -- not</p>
<p style="text-align: right;">Page 207</p> <p>1 when you're trying to trick me? 2 Q. Do you want me to give you a 3 warning before it's a trick question? 4 A. Yeah. Maybe. 5 Q. So how would you answer the 6 question does smoking cause lung cancer? 7 A. Yes. 8 Q. Even though there's some 9 types of lung cancer that it may cause 10 and there's others that it might, and it 11 might cause more than one? 12 A. There's -- 13 Q. Is that an analogy? 14 A. No, it's not an analogy. 15 Actually it makes my point quite well. 16 Because smoking causes 17 specific types of DNA changes. So the 18 carcinogenic agent in cigarette smoke 19 that causes lung cancer are benzopyrenes. 20 And there's actually a specific molecular 21 signature -- this is one of the major 22 advances that has happened in the last 23 three years primarily -- large scale 24 sequencing studies of exome sequencing,</p>	<p style="text-align: right;">Page 209</p> <p>1 all smoking-associated cancers have the 2 mutational signature of smoking. Only 3 the aerodigestive malignancies. 4 Q. So there are some type of 5 lung cancer that may be caused by smoking 6 that don't -- aren't caused by that same 7 mutation? 8 A. No, no, I didn't say that. 9 All -- 10 Q. Okay. I'm just trying to 11 understand. 12 A. All smoking-associated lung 13 cancers have the benzopyrene signature. 14 I don't remember the number. They have 15 different -- different -- there is 16 several major groups that have been doing 17 this work, and they have different 18 numbers of the signatures. 19 So actually one of the 20 references that I cite has one of the 21 numbering systems. So I can't tell you 22 the number. 23 But there's -- if you looked 24 at -- actually if you go to Cosmic, which</p>

Page 210	Page 212
<p>1 is the website in my report, it has a 2 whole section on mutational signatures 3 and it tells you which ones are smoking 4 associated.</p> <p>5 Q. And --</p> <p>6 A. And -- and the -- so the 7 small cell lung cancer, squamous cell 8 lung cancer and many but not all 9 adenocarcinomas of the lung are caused by 10 smoking largely.</p> <p>11 There are some lung cancers 12 that are probably caused by radon and 13 others that are -- we don't know the 14 pathogenesis yet.</p> <p>15 Q. What about when smoking is a 16 cocarcinogen?</p> <p>17 A. Yeah, so it's less -- 18 less -- what do you mean by cocarcinogen?</p> <p>19 Q. For example, you agree that 20 smoking and asbestos together cause -- 21 are more likely to cause cancer than 22 either by themselves?</p> <p>23 A. So smoking plus asbestos are 24 dramatically cocarcinogenic for lung</p>	<p>1 reliable?</p> <p>2 A. No. It's reliable insofar 3 as it's epidemiological evidence one way 4 or another for a particular disease.</p> <p>5 But I should add there's 6 been extensive sequencing of ovarian 7 cancers over -- I don't remember if it 8 was 400 -- I'm blocking on whether it's 9 450 or 600 cases are in the literature. 10 It's easy to find. So it's not like 11 ovarian cancer has been sequenced. 12 That's how we know that the Type 1 tumors 13 and Type 2 tumors have completely 14 different mutational profiles.</p> <p>15 Q. Okay. Well, the second 16 sentence in that paragraph is, "Studies 17 including epidemiological reports that 18 treat ovarian cancer as a single entity 19 should, in my opinion, be viewed with 20 skepticism."</p> <p>21 And I guess my question 22 would -- because we have the sequencing 23 that -- sequencing that you're referring 24 to, should epidemiological studies that</p>
Page 211	Page 213
<p>1 cancer. And I don't know if there's been 2 a detailed study of smoking plus asbestos 3 lung cancer that's been sequenced.</p> <p>4 But I would strongly suspect 5 that mutational signature of benzopyrenes 6 is there. But I don't know that. I 7 don't know if it's been done.</p> <p>8 Q. So do we need to discount 9 any literature in which sequencing has 10 not been done yet for any type of cancer?</p> <p>11 A. Discount it from the 12 standpoint of what?</p> <p>13 Q. Is it not reliable?</p> <p>14 A. It depends what the question 15 is. I mean, what aspect of the cancer 16 are you asking about?</p> <p>17 Q. I'm just asking that, if 18 literature, epidemiological literature 19 particularly, doesn't include the 20 molecular knowledge gained by sequencing 21 and other methods, should it be 22 discounted?</p> <p>23 A. Discounted in terms of what?</p> <p>24 Q. Should it not be considered</p>	<p>1 are treating ovarian cancer as a single 2 entity be discounted?</p> <p>3 A. I didn't say that.</p> <p>4 I said they should --</p> <p>5 Q. Well, I'm kind of -- I'm 6 sorry. I'm trying to --</p> <p>7 A. I stand by the wording in my 8 report.</p> <p>9 Q. Well --</p> <p>10 A. They should be viewed with 11 skepticism --</p> <p>12 Q. Well, I'm trying to --</p> <p>13 A. -- because they're not the 14 same disease.</p> <p>15 Q. I'm trying to determine what 16 you mean by "viewed as skepticism." Are 17 they less reliable --</p> <p>18 A. They are less scientifically 19 plausible.</p> <p>20 Q. They're less scientifically 21 plausible?</p> <p>22 A. It is less plausible. It is 23 implausible that a single agent acting 24 via a single carcinogenic mechanism would</p>

<p style="text-align: right;">Page 214</p> <p>1 cause dramatically different mutational 2 processes leading to dramatically 3 distinct mutational signatures. 4 Type 1 tumors and Type 2 5 tumors originate in different cell types. 6 That's pretty clear. And they have 7 dramatically different mutational 8 signatures. 9 The fact that they have 10 different mutational signatures means 11 that they're caused by different 12 molecular processes. 13 Therefore, it is highly 14 unlikely that a single agent acting via a 15 single pathogenic mechanism would lead to 16 distinct molecular signatures acting in 17 different cells of origin. 18 Q. Are there risk factors and 19 protective risk factors for epithelial 20 ovarian cancer that cross all types in 21 your opinion? 22 A. I don't really -- I can't -- 23 you know, not coming to mind right away, 24 not that I know of, no.</p>	<p style="text-align: right;">Page 216</p> <p>1 2 tumors. 2 Q. What about age? 3 A. Well, age is -- age is just 4 due to the accumulation of mutations. 5 All mutations are more common with age. 6 So age is -- age is a contributor to all 7 forms of cancer, but that's because the 8 chances of accumulating the necessary 9 mutations by any mutational process 10 increase with age. 11 Q. What about BRCA1 and 2? 12 A. BRCA1 and 2 are primarily 13 Type -- Type 2 tumors. 14 Q. And only serous? 15 A. Well, some people would 16 call, you know, the peritoneal carcinomas 17 and the carcinosarcomas separate. But I 18 think molecularly they -- most people 19 would view them as Type 2 tumors, 20 effectively the same as serous cancer, 21 yes. 22 Q. And you're including -- 23 A. High grade serous, not the 24 low grades.</p>
<p style="text-align: right;">Page 215</p> <p>1 Q. So -- 2 A. Well, so -- for example, let 3 me just -- what do you mean by all types? 4 So for example, the -- you know, obesity 5 is associated with, you know, 6 endometrioid and clear cell. But those 7 are the same type of pathogenic 8 mechanisms. 9 Q. How about the reproductive 10 risk for protective factors, for example, 11 parity, oral contraceptive use, that 12 appear to apply to all subtypes, 13 histologic subtypes, as well as Type 1 14 and Type 2. Would you agree? 15 A. Yeah, I think parity 16 probably does. But I -- that's not clear 17 that could be a single entity either. 18 That could be more than one entity. In 19 one case, it could be incessant 20 ovulation. In the other case, it could 21 be the weak -- it could be that both 22 mechanisms have been purported to explain 23 the parity effect could operate 24 differently in different Type 1 and Type</p>	<p style="text-align: right;">Page 217</p> <p>1 Q. And you're including 2 endometrioid and clear cell with the Type 3 1 tumors? 4 A. No. Oh, with the Type 1, 5 yeah. Sorry. Yeah, I'm a little -- it's 6 a little -- it's the postprandial thing. 7 I shouldn't have eaten anything. 8 Q. Let's go to your report on 9 Page 14. And you begin Section 3, talc 10 and ovarian cancer. And it looks like to 11 me this is where you put your major 12 opinions in bold. And it says "Opinion." 13 In the paragraph that 14 states, "Talc is chemically inert and 15 nongenotoxic," you have three references 16 there. 17 This morning you testified 18 that you only saw the Health Canada risk 19 assessment yesterday and that you had not 20 read it, correct? 21 A. I think that I -- I didn't 22 see the Health Canada actual text. I 23 must have seen something that said it was 24 possibly carcinogenic, but I don't know</p>

<p style="text-align: right;">Page 218</p> <p>1 where I saw that. It might be -- I'm 2 citing the paper. I think it's the 3 Taher, et al., paper. That's what I 4 assume it is. 5 Q. Well, that's what I'm trying 6 to establish. So that when you said 7 Health Canada reviewed the literature, 8 you haven't actually read the Health 9 Canada assessment, right? 10 A. I read the -- was it Taher? 11 What are you calling it? 12 Q. Taher. 13 A. Taher. I read the Taher, et 14 al., paper -- 15 Q. Okay. 16 A. -- that said that it was 17 funded by Health Canada. 18 Q. So that's -- that's wrong 19 that Health Canada reviewed the 20 literature, correct? 21 A. It says, "The Taher, et al., 22 manuscript that was funded by Health 23 Canada." 24 So that's what I'm referring</p>	<p style="text-align: right;">Page 220</p> <p>1 could have been a little bit -- 2 Q. Yeah. 3 A. -- sloppy writing. 4 Q. And it says, "It focuses 5 primarily on a meta-analysis by Taher." 6 So it -- but you're saying that you meant 7 Taher reviewed the literature, not Health 8 Canada? 9 A. Yes. 10 Q. Okay. Let's go ahead and 11 mark the three documents that you 12 referred to in that paragraph now that we 13 have it clear that it wasn't the Health 14 Canada, it was the Taher article. 15 (Document marked for 16 identification as Exhibit 17 Neel-18.) 18 BY DR. THOMPSON: 19 Q. The first is the letter that 20 you referred to as -- from the FDA to 21 Samuel Epstein will be Exhibit 18. 22 DR. THOMPSON: The IARC 23 Volume 93 published in 2010. 24 MS. SHARKO: No, no, no,</p>
<p style="text-align: right;">Page 219</p> <p>1 to. 2 Q. Okay. So is it your 3 understanding that Health Canada 4 commissioned Taher and his group to do a 5 meta-analysis, and that's what Health 6 Canada relied on in part on their risk 7 assessment, correct? 8 A. That's my understanding, 9 yes. 10 Q. But each time that you're 11 referring to Health Canada in your 12 report, you're actually referring to the 13 Taher paper? 14 A. That's correct. 15 Q. Because you have not read -- 16 actually read the Health Canada risk 17 assessment? 18 A. That's correct. I read the 19 Taher, et al., manuscript, funded by 20 Health Canada, as it says in my report. 21 Q. Okay. Well, your report 22 actually says Health Canada had reviewed 23 the literature. 24 A. So I -- maybe it was --</p>	<p style="text-align: right;">Page 221</p> <p>1 you're marking your notes. 2 DR. THOMPSON: Oh, see 3 you're looking after me. 4 MS. SHARKO: I'm watching 5 out for you. 6 (Document marked for 7 identification as Exhibit 8 Neel-19.) 9 DR. THOMPSON: 19 then will 10 be the -- will you all take all of 11 these. 12 -- will be the IARC 2010 13 monograph on non-asbestiform talc. 14 (Document marked for 15 identification as Exhibit 16 Neel-20.) 17 DR. THOMPSON: And the third 18 will be the Taher systematic 19 review and meta-analysis that was 20 commissioned by Health Canada. 21 That's all I have with that one. 22 BY DR. THOMPSON: 23 Q. So let's go to your first 24 opinion. That talc is chemically inert.</p>

Page 222	Page 224
<p>1 What do you mean by</p> <p>2 chemically inert?</p> <p>3 A. I mean it doesn't directly</p> <p>4 damage -- in the context of this</p> <p>5 statement it doesn't directly damage DNA.</p> <p>6 It doesn't cause DNA damage.</p> <p>7 Q. Is it biologically inert in</p> <p>8 your opinion, or are you -- are you using</p> <p>9 those two terms interchangeably?</p> <p>10 A. No, I'm saying the -- no,</p> <p>11 I'm not using those terms</p> <p>12 interchangeably.</p> <p>13 Q. Okay.</p> <p>14 A. In the -- in the context</p> <p>15 of -- you know, in the body it can cause</p> <p>16 granulomatous inflammation or granulomas.</p> <p>17 But that's not the kind of inflammation</p> <p>18 that's associated with carcinogenesis.</p> <p>19 But it doesn't -- it's --</p> <p>20 it's chemically inert in the sense that</p> <p>21 if you have it on the table, it's not</p> <p>22 highly reactive with, you know, typical</p> <p>23 substances. So --</p> <p>24 Q. So --</p>	<p>1 inflammatory reaction of some type in</p> <p>2 human --</p> <p>3 A. It causes -- sorry.</p> <p>4 Q. -- and animal tissues?</p> <p>5 A. It causes granulomatous</p> <p>6 reactions. Some people would call that</p> <p>7 an inflammatory reaction. Some people</p> <p>8 would call it a foreign body reaction.</p> <p>9 Some people just call it a granuloma.</p> <p>10 But it's not the kind of</p> <p>11 inflammation that Balkwill or Hanahan</p> <p>12 were referring to in terms of</p> <p>13 carcinogenesis.</p> <p>14 Q. And it certainly causes an</p> <p>15 acute inflammatory reaction as well?</p> <p>16 A. It causes granulomatous</p> <p>17 inflammation.</p> <p>18 Q. When it's used for</p> <p>19 pleurodesis, what type of reaction is it?</p> <p>20 A. It's a granulomatous and</p> <p>21 fibrotic response.</p> <p>22 Q. Okay. So granulomatous and</p> <p>23 fibrotic response.</p> <p>24 And what's your basis for</p>
Page 223	Page 225
<p>1 A. And if you put it on cells</p> <p>2 it doesn't damage DNA.</p> <p>3 Q. Okay. So to you chemically</p> <p>4 inert here is being used as not directly</p> <p>5 damaging DNA?</p> <p>6 A. Not directly or indirectly</p> <p>7 damaging DNA. And that's in the context</p> <p>8 of this statement. But it's also</p> <p>9 chemically inert in the sense that it's</p> <p>10 not highly reactive with most substances.</p> <p>11 So...</p> <p>12 Q. Okay. So not directly or</p> <p>13 indirectly damaging DNA in the cell. And</p> <p>14 not reactive chemically --</p> <p>15 A. With most substances.</p> <p>16 Q. With most substances, okay.</p> <p>17 But you would agree that</p> <p>18 it's not biologically inert?</p> <p>19 A. No, not in certain</p> <p>20 locations. It can cause -- it's a</p> <p>21 foreign body and it can cause a foreign</p> <p>22 body reaction.</p> <p>23 Q. In -- so that you -- you</p> <p>24 agree that talcum powder does cause an</p>	<p>1 your statement that that is not the type</p> <p>2 of response that Balkwill and others are</p> <p>3 talking about?</p> <p>4 A. Because the type of -- I'm</p> <p>5 aware of the literature about</p> <p>6 inflammation and cancer. And that's</p> <p>7 typically type -- you know, the sort of</p> <p>8 infiltration with activated macrophages,</p> <p>9 infiltrated neutrophils. That's not the</p> <p>10 kind of thing you get in a chronic body</p> <p>11 reaction.</p> <p>12 And there's -- and even more</p> <p>13 to the point, there's no association of</p> <p>14 granulomas with ovarian cancer that has</p> <p>15 been published to my knowledge.</p> <p>16 Q. But can you direct me to a</p> <p>17 particular article?</p> <p>18 A. I'd have to, you know, go</p> <p>19 back and look at my literature to give</p> <p>20 you a -- I can't give you that offhand.</p> <p>21 But it's general knowledge</p> <p>22 that granulomas are not associated with</p> <p>23 ovarian cancer pathogenesis.</p> <p>24 Q. But you do agree that</p>

<p style="text-align: right;">Page 226</p> <p>1 granulomas and granulomas caused by talc 2 are well reported in ovarian pathology? 3 A. No, I would not agree with 4 that at all. Absolutely not. 5 Q. You are telling me that talc 6 granulomas are not reported in ovarian 7 tissue? 8 A. Not to my knowledge. And, 9 in fact, the case -- the literature that 10 I cited in my report, I'd have to pull 11 out the exact references, reported talc 12 particles in the ovary with no associated 13 granulomatous inflammation. 14 Q. Have you looked at a GYN 15 pathology textbook lately? 16 A. I would have no occasion to 17 look at a GYN pathology textbook. 18 Q. Would it surprise you if 19 virtually every GYN pathology textbook 20 would have a section on foreign body 21 granulomas including talc? 22 A. I would have to look at 23 exactly what you're talking about. 24 Q. I didn't bring a textbook</p>	<p style="text-align: right;">Page 228</p> <p>1 form. Misstates the testimony. 2 THE WITNESS: Can you repeat 3 the question? 4 BY DR. THOMPSON: 5 Q. Well, let me just ask it. 6 Is -- is fibrous talc chemically inert? 7 A. I -- I have no specific 8 opinion on fibrous talc. My opinions 9 are -- are related to the talc that was 10 used in the papers that I reviewed and 11 the epidemiological studies that I 12 reviewed. And whatever is in those 13 products my opinion relates to. 14 Q. Okay. Is asbestos 15 chemically inert, or do you not have an 16 opinion? 17 A. I have an opinion -- it's -- 18 it's not cellularly inert. But I don't 19 have -- I don't have a great deal of 20 detailed knowledge on asbestos 21 pathogenesis. That's not the topic of my 22 research and that's not the topic of my 23 analysis for the purposes of this report. 24 Q. So for this case you are not</p>
<p style="text-align: right;">Page 227</p> <p>1 but I do have an example. 2 Do those opinions that, in 3 your words, talc is chemically inert, 4 apply to Johnson's Baby Powder in your 5 opinion? 6 A. Yes. 7 Q. And apply to Shower to 8 Shower I assume? 9 A. Yes. 10 Q. Would that opinion apply to 11 fibrous talc? 12 A. As I said earlier today, 13 I'm -- I'm referring to any of the talc 14 that was used in the studies that I 15 evaluated for the purposes of writing my 16 report. So it does not say one way or 17 the other fibrous talc. It has to do 18 with the specific experiments that are 19 cited in my report that have to do with 20 talc and ovarian cancer pathogenesis. 21 Q. So it's fair to say that you 22 don't have an opinion as to whether 23 fibrous talc is chemically inert? 24 MS. SHARKO: Object to the</p>	<p style="text-align: right;">Page 229</p> <p>1 going to be giving opinions as to the 2 cellular effects of asbestos; is that 3 fair to say? 4 A. That's correct. 5 (Document marked for 6 identification as Exhibit 7 Neel-21.) 8 BY DR. THOMPSON: 9 Q. Exhibit 21 is an article 10 titled "Foreign Body Granulomas in Normal 11 Ovaries." I don't want to spend a whole 12 lot of time with this. 13 You can look over at -- it 14 describes a study at Hopkins, published 15 in Obstetrics and Gynecology, that ACOG 16 Green Journal, that looked at 100 17 consecutive cases of oophorectomy for 18 benign disease. And they found that, I 19 believe it was 9 percent of normal 20 ovaries had cortical granulomas 21 containing a foreign body-type giant cell 22 and associated with a foreign body which 23 consisted of magnesium silicate that they 24 postulated was talc or asbestos.</p>

<p style="text-align: right;">Page 230</p> <p>1 Does that sound like a fair 2 summary of this paper? 3 A. Well, I don't know. I'd 4 have to sit here and read it to really be 5 clear. 6 I mean, you know, I'm not 7 going to be able to accept your 8 conclusions without reading the whole 9 paper. 10 Do you want me to read the 11 paper? 12 Q. Probably not. Let's see if 13 we can just find a summary statement 14 that's not mine, that's the authors. 15 A. Well, I'm not going to agree 16 until I read the whole paper. Because 17 the summary statement would be their 18 opinions of the data, not mine. 19 Q. Okay. Do you agree that 20 this paper reports foreign body 21 granulomas in normal ovaries from Johns 22 Hopkins? 23 A. That's the title of, but I 24 mean, just -- that's the title of the</p>	<p style="text-align: right;">Page 232</p> <p>1 BY DR. THOMPSON: 2 Q. Well Group 3 had granulomas. 3 Group 4 had a foreign body. 4 A. There's nothing in there 5 that says that that's caused by talc. 6 MS. SHARKO: If we're going 7 to use the paper, why don't you -- 8 BY DR. THOMPSON: 9 Q. Okay. Go ahead and take -- 10 go ahead and take a minute to review it. 11 A. All right. There's -- I 12 mean there's no evidence that this is -- 13 there's nothing that says that it's 14 caused by talc. 15 MS. SHARKO: Wait. First, 16 read the paper. Then she'll ask 17 you a question. Okay. There's no 18 question pending. I don't think. 19 DR. THOMPSON: I don't think 20 so either. But I'm not sure. 21 MS. SHARKO: Okay. Well if 22 there is, you'll ask it again. 23 BY DR. THOMPSON: 24 Q. So did this article report</p>
<p style="text-align: right;">Page 231</p> <p>1 paper. But again I just want to -- just 2 in casually pursuing it, cases, on the 3 first page, it says, "Cases in which 4 there were foci of reticular stroma with 5 or without inflammation" -- oh, sorry. 6 Q. Yeah. 7 A. "Cases in which there were 8 foci of reticular stroma with or without 9 inflammation that have been classically 10 referred to as 'cortical granulomas' but 11 have been referred to as endometriosis by 12 others." 13 And in cases, and then these 14 giant cell ones which may be cortical -- 15 which may be, you know, granulomas. 16 But there's -- it seems -- 17 Q. Well, Group -- Group 3 -- 18 MS. SHARKO: Let him finish. 19 He said, "but there." 20 THE WITNESS: Group 3 says 21 has been described -- I'm not a 22 gynecological pathologist. I 23 can't comment on whether that's 24 really endometriosis or not.</p>	<p style="text-align: right;">Page 233</p> <p>1 on foreign body granulomas that, when 2 tested using computer-assisted x-ray 3 analysis of the crystalline foreign body, 4 they were determined to be composed 5 largely of magnesium and silicone. 6 A. Yes. Okay. Well, that's 7 what the paper says. I am not an expert 8 in how one decides what a particle is. 9 So I can't comment whether this is 10 consistent with talc or not. 11 Q. Okay. 12 A. But I will -- can I finish? 13 I will notice that 14 44 percent of these patients had a 15 previous laparotomy -- a previous 16 laparotomy so that raised -- they could 17 have gotten from talc from the talcum 18 powder in the surgical gloves which was 19 probably present at the time. 20 So this is -- you know, I 21 don't think it's questionable that talc 22 can cause granulomas. The question is 23 whether perineal talc causes granulomas. 24 And there's absolutely no evidence in</p>

<p style="text-align: right;">Page 234</p> <p>1 this paper that I can see from my reading 2 that perineal talc causes granulomas in 3 the ovary. 4 Q. But talc can cause granuloma 5 in the ovary, correct? 6 A. I think that's -- yeah, talc 7 can definitely cause granulomas probably 8 in many body cavities, but I just to -- 9 can I also -- can I finish, please? 10 Q. There's no question on the 11 table. 12 A. You just asked a question. 13 Q. Well, you answered it. 14 A. No. 15 MS. SHARKO: You can -- no. 16 Finish your answer. 17 THE WITNESS: The finishing 18 of my answer is that I think the 19 relevant point is foreign body 20 granulomas in normal ovaries, 21 there's absolutely no evidence in 22 these ovaries of pre neoplastic 23 changes. So I think this actually 24 strongly supports my argument. It</p>	<p style="text-align: right;">Page 236</p> <p>1 cobalt? 2 A. As again, my opinions are 3 based on and restricted to the talc that 4 was used in the papers that I reviewed 5 and epidemiological studies that I 6 commented on in my report. So I can't 7 comment on any of these other questions 8 involving heavy metals or stuff like 9 that. 10 Q. I understand. But I'm going 11 to ask them regardless. 12 A. That's fine. 13 Q. So be patient. 14 A. I'm patient. 15 Q. So it's really irrelevant to 16 you whether or not talcum powder products 17 like Johnson's Baby Powder contain heavy 18 metals? 19 A. It's irrelevant to me in the 20 context of whether they cause ovarian 21 cancer, because I'm basing my opinion on 22 the biological experiments using said 23 products and the epidemiological studies 24 that included or were focused on mainly</p>
<p style="text-align: right;">Page 235</p> <p>1 doesn't argue against it. 2 BY DR. THOMPSON: 3 Q. Are there pre-neoplastic 4 changes that can be observed in ovaries? 5 A. In ovaries, yes. 6 Q. What are those? 7 A. So some cortical inclusion 8 cysts can show evidence of metaplastic 9 change. But I -- they didn't just remove 10 the ovaries. I assume they removed the 11 fallopian tubes too. You don't need to 12 just remove ovaries. 13 Q. You have no idea whether 14 they did or not, do you? 15 A. Well, give me some time 16 here. I don't know, but as a -- you 17 know, as a gynecological oncologist, you 18 would know that. 19 Q. And you're not a GYN 20 pathologist as you just stated? 21 A. That's correct. 22 Q. Does the opinion about talc 23 being chemically inert, would that apply 24 to heavy metals like chromium, nickel, or</p>	<p style="text-align: right;">Page 237</p> <p>1 the use of said products. 2 Q. And it's irrelevant as far 3 as a biologically plausible mechanism as 4 well. Would you agree with that 5 statement? 6 A. My evidence -- my statement 7 on biological plausibility is based on 8 the purported evidence supporting the 9 case that talc is involved in ovarian 10 cancer, based on biological experiments, 11 or the absence of proof in those 12 experiments that talc causes any evidence 13 of ovarian cancer. 14 So it's based on that. 15 Q. And are chemicals that are 16 known to be contained in Johnson's Baby 17 Powder as fragrances, would your opinion 18 that they're chemically inert also be 19 irrelevant? 20 A. I'm not aware of what 21 chemicals are or are not in Johnson's 22 Baby Powder, so I can't comment on that 23 one way or the other. 24 Q. So you don't have an opinion</p>

<p style="text-align: right;">Page 238</p> <p>1 as to whether styrene, cumarin, eugenol, 2 d-limonene, p-Cresol, musk ketone, and 3 benzophenone, which are all possible or 4 known carcinogen, would render talcum 5 powder not chemically inert? 6 MS. SHARKO: Object to the 7 form of the question. 8 BY DR. THOMPSON: 9 Q. Did you understand the 10 question? 11 A. That was sort of a double 12 negative. 13 Q. It was. 14 A. I'm trying to parse it. 15 And, you know -- 16 Q. Fair enough. 17 A. -- my blood sugar dropped 18 after lunch. 19 Q. Right. 20 A. It's hard enough. 21 Q. Are chemicals such as -- 22 that are known to be possible or 23 suspected carcinogens -- are chemicals 24 like styrene, cumarin, eugenol,</p>	<p style="text-align: right;">Page 240</p> <p>1 products are chemically inert? 2 A. No, I -- 3 MS. SHARKO: Objection. 4 Asked and answered. 5 THE WITNESS: As I explained 6 this morning it's impossible for 7 me to do any experiments under the 8 conditions of my contractual 9 obligation to be an expert witness 10 in this case. 11 So, no, I did not perform 12 any experiments, nor do I plan to. 13 BY DR. THOMPSON: 14 Q. Can you refer me to studies 15 that explicitly state that Johnson's Baby 16 Powder and Shower to Shower products are 17 chemically inert? 18 A. No, I cannot refer you to 19 studies that state that. 20 Q. Regarding your opinion, talc 21 does not cause mutations, you describe in 22 your report that cancer is a disease that 23 involves mutations and specific genes, 24 right?</p>
<p style="text-align: right;">Page 239</p> <p>1 d-limonene, p-Cresol, musk ketone, and 2 benzophenone chemically inert? 3 MS. SHARKO: I object to the 4 form of the question. It lacks 5 foundation and it assumes facts 6 not in evidence. 7 THE WITNESS: I am not a 8 toxicologist. So I can't comment 9 on any of those specific 10 chemicals. 11 BY DR. THOMPSON: 12 Q. So -- 13 A. And I don't have any 14 knowledge as to whether or not they're in 15 Johnson & Johnson products. So I can't 16 comment. 17 Q. So you would not be giving 18 any opinions as to whether those 19 chemicals that I just named off were 20 chemically inert or not? 21 A. No, I will not be giving an 22 opinion on that. 23 Q. Did you perform any studies, 24 experiments to test whether talcum powder</p>	<p style="text-align: right;">Page 241</p> <p>1 A. Yes. 2 Q. And -- 3 A. Where are we in my report, 4 please, so I can follow along. 5 Q. We're still on Page 14 with 6 those opinions -- 7 A. Oh, okay. All right. 8 Q. -- opinions in bold? 9 A. I see. Sorry, yeah. 10 Q. Do you agree that 11 carcinogens can be genotoxic or 12 non-genotoxic? 13 A. Promoters can be -- again, 14 it comes down to a little bit of a 15 semantic argument. I mean, primary 16 carcinogens are mutagens. Some people 17 would -- as I said earlier this morning, 18 some people would class tumor promoters 19 that are not direct mutagens, as 20 carcinogens. 21 So I prefer to discriminate 22 between initiating events and promotion 23 events. 24 Q. With a definition of</p>

<p style="text-align: right;">Page 242</p> <p>1 carcinogenesis that includes initiation 2 and promotion, can you agree that 3 carcinogen can either be genotoxic or 4 non-genotoxic? 5 A. Yes. 6 Q. But your opinion is for 7 initiation purposes, that carcinogens 8 have to be genotoxic; is that correct? 9 A. Yes. 10 Q. And you are 100 percent 11 confident in that opinion? 12 A. They have to be directly or 13 indirectly genotoxic. They have to cause 14 damage to DNA, otherwise they are not 15 carcinogens. 16 Q. And what do you -- what do 17 you mean by indirectly genotoxic? 18 A. If they indirectly cause 19 reactive oxygen generation and the 20 reactive oxygen species cause the -- 21 cause the mutations, that would be 22 indirectly genotoxic. 23 Q. Wouldn't -- wouldn't some 24 scientists refer to that indirect</p>	<p style="text-align: right;">Page 244</p> <p>1 epidemiological studies can address that 2 question directly. 3 Q. That -- that was -- yeah. 4 That answered my question. Thanks. 5 A. I -- well, not standard 6 epidemiological studies. New types of 7 epidemiological approaches could in 8 principle do that. But that would be a 9 new approach. 10 Q. So you're really referring 11 to the cellular studies when you give the 12 opinion that talc does not cause 13 mutation, correct? 14 A. Yes. And the fact that it 15 was tested in the Ames test for example, 16 and other standard toxicity tests. 17 Q. I'll get to that in a 18 minute. 19 Does that opinion apply to 20 asbestos? 21 A. I have no opinion 22 specifically on asbestos, as I told you 23 earlier. 24 Q. And same thing with talc</p>
<p style="text-align: right;">Page 243</p> <p>1 mechanism as non-genotoxic? 2 A. I -- I can't comment on what 3 other scientists would refer to. If you 4 want to give me a specific literature 5 reference I can help out on that. 6 Q. Okay. I may need some help 7 with that one. Because I believe that 8 I've seen that in the literature. 9 And does the opinion that 10 talc does not cause mutations apply to 11 Johnson's Baby Powder? 12 A. It applies -- my opinions 13 again -- I'm sorry to be repetitive -- 14 but my opinions refer to any of the 15 studies, epidemiological or biological, 16 that included Johnson & Johnson baby -- 17 baby product and baby -- baby shower, and 18 to talc used in said studies that was not 19 from Johnson & Johnson. 20 Q. You would agree that your 21 opinion that talc does not cause 22 mutations is not based on epidemiological 23 literature, right? 24 A. I don't believe that</p>	<p style="text-align: right;">Page 245</p> <p>1 fiber or fibrous talc? 2 A. Again, as I said earlier, my 3 comments are not relevant to that -- or 4 not -- 5 Q. How about heavy -- 6 A. My comments are not germane 7 to -- I have no comments on that. Sorry. 8 Q. And -- no apologies needed. 9 And how about the chemical 10 carcinogens that are possibly in Baby 11 Powder? 12 A. I -- 13 MS. SHARKO: Object. Object 14 to the form of the question. 15 Lacks foundation. 16 THE WITNESS: So, same -- 17 same answer as I said before. 18 My -- my opinions are restricted 19 to Johnson & Johnson products, 20 effects on cellular or animal 21 models in the context of mutation 22 generation. 23 BY DR. THOMPSON: 24 Q. And did you perform any</p>

<p style="text-align: right;">Page 246</p> <p>1 studies testing whether talcum powder 2 products cause mutations? 3 MS. SHARKO: You know, asked 4 and answered. This is about the 5 seventh time you've answered that. 6 DR. THOMPSON: The question 7 has not been -- 8 MS. SHARKO: He has not done 9 any studies other than research. 10 DR. THOMPSON: I'm -- but 11 I'm allowed to ask about a test 12 for mutations. It's not the same 13 question. 14 BY DR. THOMPSON: 15 Q. Go ahead. 16 A. I have performed no studies 17 on Johnson & Johnson Baby Powder, baby 18 showers, any Johnson & Johnson product or 19 any form of talc in my own laboratory, 20 because I am prohibited from so doing as 21 a consequence of my institution's 22 conflict of interest rules. 23 Q. Can you refer me to any 24 study that explicitly states that</p>	<p style="text-align: right;">Page 248</p> <p>1 particles and fibers? 2 MS. SHARKO: Wait. I 3 couldn't -- somebody coughed and I 4 couldn't hear the question. Can 5 you say it again? 6 BY DR. THOMPSON: 7 Q. Do you agree that standard 8 genotoxicity tests are not reliable for 9 the determination of the genotoxicity of 10 particles and fibers? 11 A. I'm not an expert on 12 toxicology. So I don't have a lot of 13 experience with genotoxicity of particles 14 and fibers. 15 But my point was that it's 16 not genotoxic, and that I stand by. 17 Q. So you're saying it's not 18 genotoxic, but you don't have any 19 experience with genotoxicity of particles 20 and fibers? 21 A. No, I'm saying that the 22 standard genotoxicity assays were done on 23 talc and it's not genotoxic. Scientists 24 reach conclusions based on assays and</p>
<p style="text-align: right;">Page 247</p> <p>1 Johnson's Baby Powder and Shower to 2 Shower don't -- do not cause mutations? 3 A. Not offhand, no. 4 Q. Your next opinion is that 5 talc is not genotoxic. And you state as 6 support of that, that -- on Page 16, that 7 "talc is universally acknowledged to be 8 non-genotoxic in standard mutagenesis 9 assays." 10 What assays are you 11 referring to? 12 A. These are the genes test 13 which is a test of mutations. I forgot 14 the name of the test, but it's a test of 15 chromosomal segregation defects. 16 Q. And you -- 17 A. Actually, I just want to 18 state that, again, all of the regulatory 19 agencies agree with that statement, 20 including the FDA, and -- well, certainly 21 IARC. 22 Q. Do you agree that standard 23 genotoxicity tests are not reliable for 24 the determination of the genotoxicity of</p>	<p style="text-align: right;">Page 249</p> <p>1 experiments, not based on suppositions or 2 hypotheses. 3 Q. My question was, are you 4 aware that the genotoxicity testing is 5 not accurate with particles and fibers? 6 MS. SHARKO: So I object to 7 the form of the question. That's 8 not what you asked him. If that's 9 your question, he'll be happy to 10 answer that. 11 DR. THOMPSON: Okay. I'll 12 ask that question then. 13 BY DR. THOMPSON: 14 Q. Are genotoxicity tests 15 accurate when testing particles and 16 fibers? 17 A. Accurate in terms of what? 18 Q. Reliable. 19 A. Reliable in terms of what? 20 Q. Well, your statement is 21 "talc is universally acknowledged to be 22 non-genotoxic in standard mutagenesis 23 assays." 24 And I'm asking you, do you</p>

<p style="text-align: right;">Page 250</p> <p>1 have knowledge regarding the reliability 2 of those tests in products that are -- 3 have particles or fibers? 4 A. The tests are extremely 5 reliable. They measure genotoxicity. 6 Whether you use a particle, fiber, any 7 chemical, they measure genotoxicity. 8 Q. Okay. 9 A. That's not -- the issue is 10 whether there are other types of assays 11 that might yield a different result, and 12 I have no expertise on particles and 13 fibers beyond the fact that standard 14 assays of genotoxicity do not show any 15 mutagenesis. 16 And that's -- that's true to 17 the best of my knowledge. 18 (Document marked for 19 identification as Exhibit 20 Neel-22.) 21 BY DR. THOMPSON: 22 Q. This is -- I just marked 23 Exhibit 22. It is an article titled 24 "Mechanisms of Genotoxicity of Particles</p>	<p style="text-align: right;">Page 252</p> <p>1 be reasonable. 2 MS. SHARKO: No, I -- I 3 disagree. I don't know that 4 that's what we've always done. If 5 you want to use your deposition 6 time to have him read it, then 7 we're not going off the record. 8 DR. THOMPSON: I'm going to 9 use my deposition time to have him 10 look at the chart on Page 70. 11 THE WITNESS: I can see the 12 chart. 13 BY DR. THOMPSON: 14 Q. Is that chart consistent 15 with what your opinions would be 16 regarding genotoxicity of particles and 17 fibers? 18 A. As I said, I'm not an expert 19 in particle and fibers. And I have no 20 comment on this paper because I would 21 have to really read the entire thing. 22 And also I would have to go through the 23 literature and see what's been written 24 since 2012 -- 2002 on this subject.</p>
<p style="text-align: right;">Page 251</p> <p>1 and Fibers." 2 Have you seen this article 3 before? 4 A. No. 5 Q. Do you -- would you like to 6 take a minute to look through it? 7 A. I mean it will take me at -- 8 at least an hour to read this paper. 9 Q. Okay. Well, we won't spend 10 an hour. Let's just go to the chart -- 11 MS. SHARKO: Well, no, it's 12 not fair to ask him about it if 13 he's not seen it before or read 14 it. 15 DR. THOMPSON: Okay. We'll 16 go off the record for an hour 17 then. It will be fine. 18 MS. SHARKO: No, why should 19 we go off the record? You want to 20 use this -- 21 DR. THOMPSON: Because 22 that's what we've always done when 23 an expert needs longer time to go 24 through an article than seems to</p>	<p style="text-align: right;">Page 253</p> <p>1 Again, 2002 is a long time 2 ago in cancer biology. And I have no 3 knowledge offhand whether this is even 4 considered to be state of the art. 5 Q. Okay. All right. We'll 6 move on. 7 A. So I have no comment. 8 Q. We'll move on. Did you 9 perform any studies to test whether 10 talcum powder products are not genotoxic? 11 MS. SHARKO: Objection. 12 Asked and answered. 13 BY DR. THOMPSON: 14 Q. You can answer again. 15 A. As I said -- 16 Q. You don't have to give the 17 explanation. Just say yes or no. 18 A. No. 19 MS. SHARKO: No, you should 20 give a complete answer. You can't 21 just keep asking a question and 22 hope for a sound bite. He hasn't 23 done any studies. We stipulated 24 that.</p>

<p style="text-align: right;">Page 254</p> <p>1 MS. O'DELL: Object to the 2 form, Susan. 3 DR. THOMPSON: Hey, I don't 4 need the -- I do not need the 5 speaking objection. 6 MS. O'DELL: Or coaching the 7 witness. 8 MS. SHARKO: He clearly 9 doesn't need coaching, especially 10 when you've asked the same 11 question like ten times. 12 MS. O'DELL: Not that that's 13 restrained you at all. It's 14 coaching the witness. Object to 15 form is the appropriate objection. 16 BY DR. THOMPSON: 17 Q. Can you refer me to any 18 studies that explicitly state that 19 Johnson & Johnson Baby Powder and Shower 20 to Shower are not genotoxic? 21 MS. SHARKO: Objection. 22 Asked and answered. 23 THE WITNESS: I think you 24 asked that already, but no.</p>	<p style="text-align: right;">Page 256</p> <p>1 humans or would that include animals as 2 well? 3 A. That would refer to both. 4 Q. You do agree, then, that 5 talcum powder is known to be inflammatory 6 in other tissues? 7 MS. SHARKO: Object to the 8 form. 9 THE WITNESS: You have asked 10 that in a different way before. 11 But let me try to give the same 12 answer so that it's clear. 13 If you inject talc into a 14 body cavity, it can cause a 15 foreign body reaction, which some 16 people cause -- call granuloma -- 17 granulomatous inflammation. 18 So yes, talc can cause 19 foreign body reactions or 20 granulomas. 21 However, to my knowledge, 22 there is no evidence that talc 23 causes other -- causes 24 cancer-associated inflammation,</p>
<p style="text-align: right;">Page 255</p> <p>1 BY DR. THOMPSON: 2 Q. And your opinion is that, on 3 Page 14, talc does not cause inflammation 4 in the female genitourinary tract. What 5 are you basing that opinion on? 6 A. I just want to clarify. I 7 was referring -- I was a little -- not 8 very clear in saying I'm referring to the 9 type of inflammation that usually is 10 associated with cancer. 11 So talc will potentially 12 cause a foreign body granuloma in the 13 female genital tract. But there's no 14 evidence that foreign body granulomas are 15 associated with ovarian cancer 16 pathogenesis. 17 So I may have been a little 18 loose with my terminology with that 19 particular part. But the point is that 20 talc does not cause precancerous 21 inflammation or cancer-promoting 22 inflammation in the female genital tract. 23 That's my point. 24 Q. Is that referring to female</p>	<p style="text-align: right;">Page 257</p> <p>1 particularly in the female genital 2 tract where the direct experiment 3 has been done and indirect 4 experiments have been done. And 5 the evidence, including some 6 evidence that you showed me, is 7 inconsonant with the idea that 8 it's causing cancer-promoting 9 inflammation. 10 BY DR. THOMPSON: 11 Q. And you're familiar with the 12 animal studies done with talc, correct? 13 A. Which animals studies? I'm 14 familiar with several animal studies. If 15 you want to cite a particular one, I'm 16 happy to talk about it. 17 (Document marked for 18 identification as Exhibit 19 Neel-23.) 20 BY DR. THOMPSON: 21 Q. I'll mark as Exhibit 23 as 22 the Keskin rat study. Have you seen this 23 one, Dr. Neel? 24 A. Yes, I cite that in my</p>

<p style="text-align: right;">Page 258</p> <p>1 report.</p> <p>2 Q. Okay. And the Keskin</p> <p>3 study -- did find that the rats that were</p> <p>4 exposed to talc had evidence of foreign</p> <p>5 body reaction and infection along with an</p> <p>6 increase in inflammatory cells in the</p> <p>7 genital tissues, right?</p> <p>8 A. So can we be -- let's --</p> <p>9 let's just go through the findings</p> <p>10 actually on page -- the first page. "In</p> <p>11 both groups exposed to talc, evidence of</p> <p>12 foreign body reaction" --</p> <p>13 MS. SHARKO: Slow down.</p> <p>14 Slow down.</p> <p>15 THE WITNESS: Sorry.</p> <p>16 -- "and infection along with</p> <p>17 an increase in inflammatory</p> <p>18 cells."</p> <p>19 So again, foreign body</p> <p>20 reaction I've already stipulated</p> <p>21 can be caused by talc. However,</p> <p>22 the infection causes the</p> <p>23 inflammation.</p> <p>24 So I mean, these rats got</p>	<p style="text-align: right;">Page 260</p> <p>1 the infection came from, correct?</p> <p>2 A. No. But I do know that</p> <p>3 infections cause inflammatory cells to</p> <p>4 come there. So you can't conclude</p> <p>5 anything about the nature of the</p> <p>6 inflammation. If you have an infection,</p> <p>7 you will definitely get white blood cells</p> <p>8 coming in, as any first year medical</p> <p>9 student knows.</p> <p>10 Q. Are you familiar with the</p> <p>11 Hamilton study?</p> <p>12 A. Yes.</p> <p>13 Q. Another rat study.</p> <p>14 (Document marked for</p> <p>15 identification as Exhibit</p> <p>16 Neel-24.)</p> <p>17 BY DR. THOMPSON:</p> <p>18 Q. And in this study with</p> <p>19 rats --</p> <p>20 MR. ZELLERS: Is this</p> <p>21 Exhibit 24?</p> <p>22 DR. THOMPSON: I'm sorry.</p> <p>23 Yes, Exhibit 24.</p> <p>24 BY DR. THOMPSON:</p>
<p style="text-align: right;">Page 259</p> <p>1 infected. So infection will cause</p> <p>2 inflammation. But talc is not</p> <p>3 known to cause infection, as far</p> <p>4 as I know.</p> <p>5 So this study is not</p> <p>6 relevant to the issue, except for</p> <p>7 the fact that it does cause</p> <p>8 granulomas, which was seen in</p> <p>9 other studies.</p> <p>10 BY DR. THOMPSON:</p> <p>11 Q. So you think that the</p> <p>12 infection is -- that resulted in these</p> <p>13 animals were completely unrelated to the</p> <p>14 talc?</p> <p>15 A. I can't comment on what the</p> <p>16 sterile technique was in this laboratory</p> <p>17 or what other agents they were exposed to</p> <p>18 in this laboratory.</p> <p>19 But I think that it's not</p> <p>20 alleged as far as I understand that talc</p> <p>21 causes infections as part of the</p> <p>22 plaintiffs' case.</p> <p>23 Q. So you don't know one way or</p> <p>24 the other, as far as this study, where</p>	<p style="text-align: right;">Page 261</p> <p>1 Q. The treated animals showed</p> <p>2 focal areas of papillary change on the</p> <p>3 surface epithelium, correct?</p> <p>4 A. That's what they reported,</p> <p>5 yes.</p> <p>6 Q. The authors did not conclude</p> <p>7 that the papillary changes represented</p> <p>8 first stage in development of a surface</p> <p>9 papillary epithelial neoplasm, right?</p> <p>10 A. Excuse me? Can you repeat</p> <p>11 the question.</p> <p>12 Q. Yeah, the authors --</p> <p>13 A. And what review? Refer</p> <p>14 me --</p> <p>15 Q. Well, let's just -- let's</p> <p>16 just read the authors' conclusions.</p> <p>17 A. Sure.</p> <p>18 Q. We'll just leave it at that</p> <p>19 one. I can't find my spot.</p> <p>20 You mentioned earlier that</p> <p>21 you did not know why the FDA removed</p> <p>22 powder from exam and surgical gloves,</p> <p>23 right?</p> <p>24 A. I didn't know that the FDA</p>

<p style="text-align: right;">Page 262</p> <p>1 did it, and I certainly didn't know why 2 they did it. 3 (Document marked for 4 identification as Exhibit 5 Neel-25.) 6 BY DR. THOMPSON: 7 Q. Exhibit 25 is the FDA 8 register. 9 MR. ZELLERS: Do you have 10 copies? 11 DR. THOMPSON: Oh, I do. 12 Sorry. 13 BY DR. THOMPSON: 14 Q. Beginning on the bottom 15 right of that first page, "Banned 16 devices, powdered" -- sugar -- "surgeon's 17 gloves, powdered patient examination 18 gloves and absorbable powder for 19 lubricating surgeon's glove." 20 So does that tell you that 21 the FDA banned powder use on gloves? 22 A. Sounds like it. 23 MS. SHARKO: But again, he 24 hasn't seen this. If you want to</p>	<p style="text-align: right;">Page 264</p> <p>1 A. Yes. December 2016. 2 Q. And in the first paragraph 3 on purpose, in the executive summary the 4 document states, "However" -- well, sorry 5 about that. 6 "Various types of powder 7 have been used to lubricate gloves so 8 that wearers could don the gloves more 9 easily." 10 MS. SHARKO: Wait, where are 11 you? 12 THE WITNESS: The bottom -- 13 DR. THOMPSON: The bottom of 14 the first paragraph under 15 executive summary, "Purpose and 16 coverage of the final rule." 17 BY DR. THOMPSON: 18 Q. "However, the use of powder 19 on medical gloves presents numerous risks 20 to patients and healthcare workers, 21 including inflammation, granulomas and 22 respiratory allergic reactions." 23 Did I read that right? 24 A. You read it right. But it's</p>
<p style="text-align: right;">Page 263</p> <p>1 -- 2 DR. THOMPSON: Well, he can 3 tell me if he needs to -- he can 4 tell me if he needs to see it. 5 He doesn't even know how -- 6 what my question is going to be. 7 The first was what was the 8 title of the regulation. 9 THE WITNESS: The title is 10 "Banned devices: Powdered 11 surgeon's gloves, powdered patient 12 examination gloves, and absorbable 13 powder for lubricating a surgeon's 14 gloves." 15 BY DR. THOMPSON: 16 Q. So I -- I read it correctly 17 too, right? 18 A. I think so. 19 Q. And this was published 20 December 19th of 2016, right? 21 A. Oh, I'm sorry, you're 22 asking? December -- where does it say 23 where it's published? 24 Q. At the top of the page.</p>	<p style="text-align: right;">Page 265</p> <p>1 a poorly written sentence, so it's not 2 clear what refers to what. 3 Q. But it states that 4 inflammation was -- and granulomas were 5 at least part of the reason why powder 6 was removed from surgical gloves and 7 examination gloves, right? 8 A. So the way the -- the way 9 the sentence is written is not very 10 accurate. So it's not clear whether they 11 are saying inflammation of a different 12 type and the granulomas. Or whether 13 they're -- they're basically saying 14 they're both saying the same thing. 15 And it's also not saying 16 whether the risk is to the patient or to 17 the healthcare worker. And it's also not 18 saying that it involves talc. 19 So it's a very poorly 20 written sentence that doesn't allow me to 21 offer a very precise opinion which 22 scientists like to do. 23 Q. Okay. You cite I believe 24 the Heller study as evidence that talc</p>

<p style="text-align: right;">Page 266</p> <p>1 does not have an inflammatory effect on 2 the ovaries, right?</p> <p>3 A. I cite two studies. But one 4 of them is Heller, yes.</p> <p>5 Q. Are you aware that Heller 6 only looked at one specimen out of 24 7 histologically?</p> <p>8 A. I'd have to go back and look 9 at the paper again.</p> <p>10 Q. If Heller only looked at one 11 specimen, would that be evidence of what 12 was in the other 23 specimens?</p> <p>13 MS. SHARKO: Can we get a 14 copy of Heller? Please?</p> <p>15 (Document marked for 16 identification as Exhibit 17 Neel-26.)</p> <p>18 BY DR. THOMPSON:</p> <p>19 Q. This will be Exhibit 26, 20 Heller paper, "The Relationship Between 21 Perineal Cosmetic Talc Usage and Ovarian 22 Talc Particles."</p> <p>23 MS. SHARKO: Thank you.</p> <p>24 BY DR. THOMPSON:</p>	<p style="text-align: right;">Page 268</p> <p>1 paper that they looked at any sections 2 using H&E light microscopy besides this 3 one --</p> <p>4 A. It's not clear from the way 5 this is written that that's the only -- 6 that they are saying that it -- from -- 7 that those are the only analyzed 8 sections. But, you know.</p> <p>9 Q. But -- but you can conclude 10 from your reading of this that Heller 11 found no inflammatory reaction in the 12 ovaries of cells with -- of -- in the 13 ovaries of these subjects that they found 14 talc?</p> <p>15 A. Well, they don't report on 16 it, so it's not evidence that there is 17 inflammation in the ovary.</p> <p>18 Q. Well, you cited this paper, 19 right?</p> <p>20 A. Yeah, I did cite to it --</p> <p>21 Q. For that purpose?</p> <p>22 A. Yeah. I said that there was 23 no evidence.</p> <p>24 Q. And you'll agree that there</p>
<p style="text-align: right;">Page 267</p> <p>1 Q. And I'm looking at the last 2 paragraph of the results section, 3 Dr. Neel.</p> <p>4 And it says, "In one subject 5 we studied both ovaries. On the right 6 side we detected no talc. On the left 7 side" -- "by electron microscopy and 556 8 particles by light microscopy. And on 9 the left side we detected 1,669,000 10 particles per gram of wet weight by 11 electron microscopy and six particles by 12 light microscopy.</p> <p>13 "Hematoxylin and Eosin 14 stained slides from the analyzed sections 15 of tissues were examined. There was no 16 evidence of response to talc such as 17 foreign body giant cell reactions or 18 fibrosis in the tissue."</p> <p>19 A. It's -- I mean, it's not 20 clear to me whether they only looked at 21 those, at the sections from the -- the 22 one subject above or not. Or whether 23 they looked at all of them.</p> <p>24 Q. Do you see anywhere in the</p>	<p style="text-align: right;">Page 269</p> <p>1 is no evidence of more than one being 2 looked at, right?</p> <p>3 A. As I said, I can't tell from 4 the way that's written whether it was all 5 of them or not. The major point for 6 citing this was that there was no 7 correlation between reported perineal 8 talc use and the presence of particles 9 assumed to be or -- or argued to be talc 10 in the ovaries. That was the major 11 reason for citing it.</p> <p>12 Q. While we are on --</p> <p>13 A. We already have direct 14 evidence on the animal studies about what 15 talc does in ovaries.</p> <p>16 Q. You cited the paper.</p> <p>17 A. I did and I said --</p> <p>18 Q. Okay.</p> <p>19 A. -- that they argued strongly 20 that perineal talc use does not 21 accurately reflect potential exposure. 22 And I stand by that statement. That's 23 exactly what the paper concludes.</p> <p>24 Q. While we are on the Heller</p>

<p style="text-align: right;">Page 270</p> <p>1 paper.</p> <p>2 Do you intend to give</p> <p>3 opinions as to whether perineal talc</p> <p>4 powder can migrate or be transported to</p> <p>5 the distal fallopian tube, ovary or</p> <p>6 perineal cavity?</p> <p>7 A. I intend to say that the</p> <p>8 evidence is inconclusive.</p> <p>9 Q. So you will say -- you will</p> <p>10 say that there is evidence on both sides?</p> <p>11 A. I say the preponderance of</p> <p>12 the evidence is negative.</p> <p>13 Q. What do you use for the</p> <p>14 preponderance of the evidence being</p> <p>15 negative?</p> <p>16 A. The best -- the best study</p> <p>17 is one that was done in monkeys by</p> <p>18 Whelan. All of the other studies are</p> <p>19 potentially confounded by artifact.</p> <p>20 Q. Is -- is it plausible that</p> <p>21 talcum powders -- talcum powder applied</p> <p>22 to the perineum can reach the fallopian</p> <p>23 tube, ovary and perineal cavity?</p> <p>24 A. Is it plausible? I think</p>	<p style="text-align: right;">Page 272</p> <p>1 there exists.</p> <p>2 "While there exists no</p> <p>3 direct proof of talc and ovarian</p> <p>4 carcinogenesis, the potential for</p> <p>5 particulates to migrate from the perineum</p> <p>6 and vagina to the perineal cavity is</p> <p>7 indisputable. It is, therefore,</p> <p>8 plausible that perineal talc and other</p> <p>9 particulate that reach the endometrial</p> <p>10 cavity, fallopian tubes, ovaries and</p> <p>11 peritoneum may elicit a foreign body type</p> <p>12 reaction and inflammatory response that</p> <p>13 in some exposed women may progress to</p> <p>14 epithelial cancers.</p> <p>15 "However, there was no</p> <p>16 conclusive evidence to support</p> <p>17 causality."</p> <p>18 MS. SHARKO: There has been.</p> <p>19 DR. THOMPSON: "Has been no</p> <p>20 conclusive evidence to support</p> <p>21 causality."</p> <p>22 BY DR. THOMPSON:</p> <p>23 Q. So even though the FDA</p> <p>24 determined that the potential for the</p>
<p style="text-align: right;">Page 271</p> <p>1 it's unresolved. I can't say it's</p> <p>2 plausible or implausible. It's</p> <p>3 unresolved. It's -- it's unresolved.</p> <p>4 The strongest evidence says no.</p> <p>5 Q. And you cite as -- the -- as</p> <p>6 part of your opinions, this FDA citizen's</p> <p>7 response letter, correct?</p> <p>8 A. Mm-hmm.</p> <p>9 Q. And it's marked as exhibit</p> <p>10 something.</p> <p>11 I didn't write it on the</p> <p>12 thing.</p> <p>13 If you go to the --</p> <p>14 MS. SHARKO: Go to exhibit</p> <p>15 something?</p> <p>16 BY DR. THOMPSON:</p> <p>17 Q. Give it -- go to exhibit</p> <p>18 something and we'll take a break after.</p> <p>19 MR. ZELLERS: It's 18.</p> <p>20 DR. THOMPSON: Exhibit 18.</p> <p>21 Thank you, Mr. Zeller.</p> <p>22 BY DR. THOMPSON:</p> <p>23 Q. And on Page 5, I'm reading</p> <p>24 the paragraph that starts with while</p>	<p style="text-align: right;">Page 273</p> <p>1 particulates to migrate is indisputable,</p> <p>2 you're still saying that the</p> <p>3 preponderance of the evidence based on</p> <p>4 one monkey study is against it?</p> <p>5 A. Well, it's not one monkey</p> <p>6 study, first of all. It's two monkey</p> <p>7 studies. And one --</p> <p>8 Q. But by the same -- by the</p> <p>9 same Johnson & Johnson consultant, right?</p> <p>10 A. He's -- I don't know that</p> <p>11 they're a Johnson & Johnson consultant.</p> <p>12 Q. Did you look at the conflict</p> <p>13 of interest disclosure?</p> <p>14 A. No, I didn't. But it's --</p> <p>15 the study was done in the more accurate</p> <p>16 way than the other two studies. And it</p> <p>17 actually produced very clear evidence of</p> <p>18 potential confounding artifact in the --</p> <p>19 in the studies that have been done</p> <p>20 before.</p> <p>21 Q. So --</p> <p>22 MS. SHARKO: Wait. Let him</p> <p>23 finish.</p> <p>24 THE WITNESS: So the fact is</p>

<p style="text-align: right;">Page 274</p> <p>1 that one very well-designed study 2 beats multiple poorly designed 3 studies in science. It's not a 4 plebiscite. 5 BY DR. THOMPSON: 6 Q. You're saying that two 7 monkey studies by a Johnson & Johnson 8 consultant outweigh a vast body of 9 literature on various substances, 10 including particulates being transported, 11 migrating to the ovaries, to reach your 12 conclusion that the preponderance of the 13 evidence is against migration or 14 transport to particles? 15 MS. SHARKO: I object to the 16 form of the question. Lacks 17 foundation. 18 THE WITNESS: You haven't 19 provided me with any -- vast 20 literature? You provided me with 21 two poorly designed studies. So I 22 don't know what you're talking 23 about. If you want to show me 24 other studies, I'll be happy to</p>	<p style="text-align: right;">Page 276</p> <p>1 know of something that I don't know. But 2 what I'm saying is this -- this -- 3 this -- you can't just make a statement 4 without referencing it and then assume 5 that -- and assume that scientists are 6 going to take it at face value. We have 7 to see the evidence. That's what we work 8 with, evidence. 9 Q. You really need evidence to 10 show that something can go from the 11 perineum through the genital tract? 12 A. Well, sperm can go there. 13 But they have -- but they have, you know, 14 flagella. I'm not aware of talc having 15 flagella. 16 Q. Okay. Are you aware of the 17 sperm studies that show dead sperm and 18 sperm particles can migrate through the 19 genital tract? 20 A. I don't know what studies 21 you are talking about. But if you want 22 to give me studies -- 23 Q. Okay. Let me get them. 24 A. -- I'll be happy to look at</p>
<p style="text-align: right;">Page 275</p> <p>1 read them and give my opinion on 2 them. 3 However, it is well known 4 that particle -- that radioactive, 5 you know, materials can leach off 6 of albumin particles. And also 7 the study showing that carbon 8 black is present -- it is true 9 that the Egli study did not use -- 10 did not do a control where they 11 just used the solutions 12 themselves. 13 So again the point raised by 14 Whelan is a reasonable point, 15 whether he's a consultant for 16 Johnson & Johnson or not. Science 17 is science. It doesn't matter who 18 does it. 19 BY DR. THOMPSON: 20 Q. Are the FDA not scientists 21 that say it's indisputable? 22 A. I don't know what -- the FDA 23 doesn't reference anything here, so I 24 can't comment on the studies. Maybe they</p>	<p style="text-align: right;">Page 277</p> <p>1 studies and -- 2 Q. We'll take a break and get 3 them. 4 A. -- see if I think they are 5 reliable. 6 Q. Okay. We'll take a break 7 and come back and go through the studies. 8 THE VIDEOGRAPHER: The time 9 is 2:10 p.m. Off the record. 10 (Short break.) 11 THE VIDEOGRAPHER: We are 12 back on the record. The time is 13 2:28 p.m. 14 BY DR. THOMPSON: 15 Q. Dr. Neel, has your research 16 over the last 30 years -- plus years, had 17 anything at all to do with the physiology 18 of the female genital tract? 19 A. No. 20 Q. Have you written any papers 21 that have anything to do with the 22 physiology of the female genital tract? 23 A. No. 24 Q. Prior to being contacted by</p>

<p style="text-align: right;">Page 278</p> <p>1 the lawyers in this case, did you have</p> <p>2 any knowledge of the literature regarding</p> <p>3 the potential migration or transport of</p> <p>4 particles through the female genital</p> <p>5 tract?</p> <p>6 A. Only sperm.</p> <p>7 Q. Only?</p> <p>8 A. Only sperm.</p> <p>9 Q. Only sperm. And were you</p> <p>10 aware of the literature regarding sperm</p> <p>11 particles or dead sperm being transported</p> <p>12 through the genital tract?</p> <p>13 A. No.</p> <p>14 Q. Were you aware of the</p> <p>15 literature that sperm moved more quickly</p> <p>16 through the genital tract than would be</p> <p>17 expected just from the motility of the</p> <p>18 flagella?</p> <p>19 A. I'm not aware of any studies</p> <p>20 on that issue.</p> <p>21 Q. Did you have any knowledge</p> <p>22 of the concept of the uterine peristaltic</p> <p>23 pump, which actually facilitates the</p> <p>24 migration or transport of particles?</p>	<p style="text-align: right;">Page 280</p> <p>1 A. I think anybody who has gone</p> <p>2 to medical school is pretty familiar with</p> <p>3 the general anatomy of the genital tract.</p> <p>4 Q. You don't think</p> <p>5 gynecologists have a more in-depth</p> <p>6 understanding of anatomy than other</p> <p>7 non-GYN doctors?</p> <p>8 A. I think they do have a more</p> <p>9 detailed understanding of anatomy. That</p> <p>10 doesn't necessarily mean they have a more</p> <p>11 detailed understanding of anatomy that is</p> <p>12 necessary to make a conclusion about</p> <p>13 particles moving through the genital</p> <p>14 tract. That doesn't require a very</p> <p>15 complex surgical description of the</p> <p>16 genital tract.</p> <p>17 Q. Do they have more</p> <p>18 understanding of the physiology of the</p> <p>19 reproductive tract?</p> <p>20 A. I would hope so, yeah.</p> <p>21 Q. Let's go to the Taher</p> <p>22 article. That would be Exhibit --</p> <p>23 A. 20.</p> <p>24 MS. SHARKO: 20.</p>
<p style="text-align: right;">Page 279</p> <p>1 A. Not that I recall.</p> <p>2 Q. Would you agree that a</p> <p>3 gynecologist or GYN oncologist would have</p> <p>4 a greater understanding of the migration</p> <p>5 or transport of particles through the</p> <p>6 genital tract?</p> <p>7 A. They might have a greater</p> <p>8 understanding of what's published in</p> <p>9 textbooks, but they wouldn't necessarily</p> <p>10 be any better than I am at evaluating</p> <p>11 literature on the subject.</p> <p>12 Q. But they would have more</p> <p>13 firsthand knowledge and experience --</p> <p>14 A. As I said.</p> <p>15 Q. -- in their practice,</p> <p>16 wouldn't they?</p> <p>17 A. I don't think the practice</p> <p>18 of gynecological oncology addresses the</p> <p>19 issue of the migration of particles</p> <p>20 through the genital tract. So I don't</p> <p>21 think so necessarily, no.</p> <p>22 Q. They would be more familiar</p> <p>23 with the anatomy of the genital tract,</p> <p>24 right?</p>	<p style="text-align: right;">Page 281</p> <p>1 BY DR. THOMPSON:</p> <p>2 Q. 20. And this -- this is the</p> <p>3 article that you were referring to in</p> <p>4 your report when you referenced Health</p> <p>5 Canada, right?</p> <p>6 A. Yes. And now I -- now I</p> <p>7 recall where my statement came from in my</p> <p>8 report.</p> <p>9 So if you look at the bottom</p> <p>10 of Page 1, it says, "For information</p> <p>11 contact Dr. Donald R. Mattison." It has</p> <p>12 his contact information. And it says,</p> <p>13 "Materials submitted to Health Canada."</p> <p>14 So that was where I got the</p> <p>15 information that this was commissioned by</p> <p>16 Health Canada. I may have misinterpreted</p> <p>17 that. But that's where I got the</p> <p>18 information from. And I think there's an</p> <p>19 allusion to that also in the end. But</p> <p>20 I'd have to look through it. If you want</p> <p>21 me to, I will.</p> <p>22 Q. Let's go to the chart on</p> <p>23 Page 26. And --</p> <p>24 A. Hold on. I'm not there yet.</p>

<p style="text-align: right;">Page 282</p> <p>1 That in the middle of a chart. It's the 2 middle of the chart. Do you want to 3 just -- 4 Q. 26. 5 A. -- on Page 26. 6 Q. I want to look at the -- 7 A. It continues on three pages. 8 Q. Yeah, I want to look at the 9 biological plausibility -- 10 A. Okay. 11 Q. -- section of the chart on 12 Page 26. 13 And this Taher article 14 states, under biological plausibility, 15 "Particles of" -- "of talc appear to 16 migrate into the pelvis and ovarian 17 tissue causing irritation and 18 inflammation." 19 Do you agree that that's a 20 biologically plausible mechanism? 21 A. If the data supporting it 22 were convincing, or even close to 23 convincing, yes. But they are not. 24 And so I agree that</p>	<p style="text-align: right;">Page 284</p> <p>1 A. So actually, if you look at 2 the report somewhere else, it says that 3 data on talc migration are inconsistent. 4 So we'll have to go through the entire 5 report to find that sentence. 6 But I don't think that you 7 should take this chart or this table and 8 state that as what the conclusion of the 9 report is because it's out of context. 10 Q. Well, this is Dr. Taher's 11 chart that is titled "Summary of 12 Evidence." 13 A. Well, Dr. Taher also wrote 14 that data on talc migration were 15 inconsistent. So we can look through it 16 and find out where that is, but I 17 wouldn't put that in my report unless I 18 saw it in this paper. 19 And Dr. Taher, I believe, is 20 an epidemiologist. So he -- he's not 21 really qualified to comment on biological 22 plausibility based on cellular mechanisms 23 anyway. 24 Q. So in your opinion, an</p>
<p style="text-align: right;">Page 283</p> <p>1 conceptually that would be a reasonable 2 mechanism. But they don't have -- the -- 3 the actual studies are poor or 4 nonexistent in terms of evidence. 5 Q. So your opinion, with that 6 first statement, is you would need 7 convincing evidence to have that be a 8 biologically plausible mechanism? 9 A. I would need some 10 scientifically credible evidence. All of 11 the publications that I have -- that I 12 have found that address this issue, and 13 I'm happy to review other ones with you, 14 all of the ones that I've found are 15 really poor or they don't say that this 16 is true. 17 Q. The second one, bullet point 18 under biologically -- biological 19 plausibility says, "Transport of talc via 20 perineal stroma and presence in ovaries 21 documented." 22 Do you agree that that is a 23 biologically plausible part of the 24 mechanism?</p>	<p style="text-align: right;">Page 285</p> <p>1 epidemiologist is not qualified to 2 testify as to cellular mechanisms? 3 A. Unless they are trained in 4 cellular molecular biology as well, no. 5 Q. Okay. Do you disagree with 6 the authors of the Taher paper? 7 A. What -- which parts of the 8 authors they state in these statements? 9 Q. In this biological 10 plausibility section. 11 A. I think that, yes, I do 12 disagree with several of the statements 13 in the biological plausibility section. 14 Including the particles of talc appear to 15 migrate to the pelvis and ovarian tissue, 16 I think that remains unclear. 17 The fact that they cause 18 irritation and inflammation. Particles 19 of talc cause granulomas. There's no -- 20 I don't know what irritation means. 21 That's not a scientific term as you know. 22 And transport of talc via 23 perineal stroma. I don't really know 24 what perineal stroma means. Stroma</p>

<p style="text-align: right;">Page 286</p> <p>1 actually is something that is</p> <p>2 subepithelial, so I don't know what that</p> <p>3 refers to. It's probably a misprint.</p> <p>4 And presence in the ovaries</p> <p>5 documented. We've already discussed</p> <p>6 presence in the ovaries. But we haven't</p> <p>7 established that that is from transport.</p> <p>8 Q. Could -- could evidence be</p> <p>9 inconclusive and both sides be plausible</p> <p>10 in your mind?</p> <p>11 A. Can evidence be inconclusive</p> <p>12 and plausible at the same time? No.</p> <p>13 Q. So if you have differing</p> <p>14 evidence on an issue, neither one could</p> <p>15 be plausible, is that your opinion?</p> <p>16 A. No. Good evidence is</p> <p>17 plausible. Bad evidence is not. It's</p> <p>18 not a plebiscite. It's not an election.</p> <p>19 It's not like you get a bunch of people</p> <p>20 on one side and a bunch of people on the</p> <p>21 other, and you take testimony and -- and</p> <p>22 you tally up who gets what.</p> <p>23 It's which evidence is</p> <p>24 plausible scientifically and that has to</p>	<p style="text-align: right;">Page 288</p> <p>1 Science, Engineering, Medicine, and</p> <p>2 supported by the CDC, that was a book</p> <p>3 actually titled "Ovarian Cancer:</p> <p>4 Evolving paradigms in research and care."</p> <p>5 Correct? Do you remember</p> <p>6 that?</p> <p>7 A. You'll have to show --</p> <p>8 MS. SHARKO: Object to the</p> <p>9 form of the question.</p> <p>10 THE WITNESS: I said I had</p> <p>11 seen several, you know, summary</p> <p>12 reviews.</p> <p>13 You'd have to show me the</p> <p>14 exact.</p> <p>15 BY DR. THOMPSON:</p> <p>16 Q. I will. I just -- I had</p> <p>17 remembered this morning that you were</p> <p>18 aware that this had been published. But</p> <p>19 I'm going to show it to you regardless.</p> <p>20 (Whereupon, a discussion was</p> <p>21 held off the record.)</p> <p>22 DR. THOMPSON: 27.</p> <p>23 Exhibit 27 will be "Ovarian</p> <p>24 Cancer: Evolving paradigms in</p>
<p style="text-align: right;">Page 287</p> <p>1 do with the quality of the data and the</p> <p>2 convincingness of the evidence. And</p> <p>3 that's not a plebiscite.</p> <p>4 Q. So -- so you don't see a</p> <p>5 situation where the evidence could be</p> <p>6 credible on both sides of a scientific</p> <p>7 question?</p> <p>8 A. If two people do the same</p> <p>9 experiment and they get different</p> <p>10 results, and neither one -- and there --</p> <p>11 if two people do the same experiment and</p> <p>12 they get different results, one of them</p> <p>13 is right and one of them is wrong.</p> <p>14 That's the essence of</p> <p>15 science. It's empirically observable and</p> <p>16 reproducible. So that's my opinion.</p> <p>17 Q. So science is either right</p> <p>18 or wrong?</p> <p>19 A. Or good or bad. Yes.</p> <p>20 Science is either right or</p> <p>21 wrong by definition.</p> <p>22 Q. You mentioned earlier that</p> <p>23 you are at least aware of the treatise</p> <p>24 commissioned by the National Academies of</p>	<p style="text-align: right;">Page 289</p> <p>1 research and care."</p> <p>2 (Document marked for</p> <p>3 identification as Exhibit</p> <p>4 Neel-27.)</p> <p>5 BY DR. THOMPSON:</p> <p>6 Q. I did not print the whole</p> <p>7 book. I did print the entire chapter</p> <p>8 that I'm going to be referencing.</p> <p>9 And --</p> <p>10 MR. ZELLERS: Margaret, do</p> <p>11 you have one more of them?</p> <p>12 DR. THOMPSON: I don't. I</p> <p>13 just -- oh, I do. I'm sorry.</p> <p>14 MS. SHARKO: Do you have a</p> <p>15 paperclip? May I have that</p> <p>16 paperclip?</p> <p>17 DR. THOMPSON: You are so</p> <p>18 demanding.</p> <p>19 MS. SHARKO: Thank you.</p> <p>20 BY DR. THOMPSON:</p> <p>21 Q. And on page little Roman</p> <p>22 numeral ix preface, "This congressionally</p> <p>23 mandated report sponsored by the Centers</p> <p>24 for Disease Control and Prevention</p>

<p style="text-align: right;">Page 290</p> <p>1 assesses the state of research on ovarian 2 cancers from multiple perspectives and by 3 multiple disciplines." 4 Did I read that right, the 5 first sentence of -- 6 A. Yeah. 7 Q. -- of -- 8 A. I have not seen this report 9 before, so -- 10 Q. Okay. 11 A. -- just so you know. 12 Q. And this paper -- or this 13 book actually, was authored by a 14 committee of -- approximately 15 authors, 15 correct? 16 A. Yes. 17 Q. And this book also was 18 reviewed by another, it looks like ten or 19 so reviewers, correct? 20 A. Yes. 21 MS. SHARKO: Just for the 22 record, we don't have a book in 23 front of us. We have -- 24 DR. THOMPSON: Okay. The</p>	<p style="text-align: right;">Page 292</p> <p>1 It's an observation. 2 DR. THOMPSON: Well, we 3 don't need your speaking 4 observation. Dr. Neel can -- can 5 let me know if he needs time to 6 look at whatever it is I'm showing 7 him. 8 BY DR. THOMPSON: 9 Q. Dr. Neel, this section on 10 Page 110 titled "Inflammation" is under 11 the heading behavioral and inflammatory 12 risk factors. 13 And I'm going to read the 14 first part of this paragraph. "Studies 15 of the inflammatory marker C-reactive 16 protein suggest a possible association 17 between inflammation and an increased 18 risk of ovarian cancer." There are two 19 cites. 20 "Other specific inflammatory 21 factors have also been associated with 22 ovarian cancer. A meta-analysis reported 23 that exposure to asbestos was associated 24 with a 77 percent increased risk of</p>
<p style="text-align: right;">Page 291</p> <p>1 chapter from the book. 2 MS. SHARKO: Okay. Thank 3 you. 4 BY DR. THOMPSON: 5 Q. Let's go to -- and this, the 6 chapter that I did take from this book is 7 titled "Prevention and Early Detection." 8 And if you'll go to 9 Page 110. The topic heading -- 10 A. Okay. I see the numbers 11 now. 12 MS. SHARKO: And the witness 13 should have the opportunity -- 14 DR. THOMPSON: Susan, we 15 don't need any speaking 16 objections. How many times do we 17 need to tell you that? 18 MS. SHARKO: Well, I'll 19 ignore -- 20 DR. THOMPSON: And there -- 21 the witness is perfectly -- 22 MS. SHARKO: I'll ignore 23 your rudeness. It's not an -- 24 it's not -- it's not an objection.</p>	<p style="text-align: right;">Page 293</p> <p>1 ovarian cancer mortality," citing 2 Camargo, "and the International Agency 3 for Research on Cancer determined that 4 there was sufficient evidence to support 5 a causal relationship between asbestos 6 exposure and ovarian cancer," citing 7 Straif. 8 "This has led to studies of 9 talc use, which is chemically similar to 10 asbestos and can cause an inflammatory 11 response. The use of talcum powder has 12 been associated with a 20 to 30 percent 13 increased risk of ovarian cancer, 14 although it has been shown" -- "show to 15 vary by histologic subtype." 16 Did I read that correctly? 17 MS. SHARKO: No. You left 18 out the word "perineal." 19 THE WITNESS: Yeah, perineal 20 talc. 21 BY DR. THOMPSON: 22 Q. Okay. Thank you. Anything 23 else? 24 A. I think you read that</p>

<p style="text-align: right;">Page 294</p> <p>1 correctly.</p> <p>2 Q. Okay. So the state of the</p> <p>3 art committee that was commissioned by</p> <p>4 the National Academy of Science</p> <p>5 Medicine -- are you familiar with that</p> <p>6 organization?</p> <p>7 MR. LOCKE: Objection.</p> <p>8 THE WITNESS: Yes. I hope</p> <p>9 to be in it.</p> <p>10 What was that?</p> <p>11 MR. LOCKE: I just said</p> <p>12 objection.</p> <p>13 THE WITNESS: Okay.</p> <p>14 BY DR. THOMPSON:</p> <p>15 Q. And it has a reputation</p> <p>16 certainly, correct?</p> <p>17 A. Yes. I know most of the</p> <p>18 people on this panel.</p> <p>19 Q. Do you know -- do you know</p> <p>20 the authors?</p> <p>21 A. I know several of them.</p> <p>22 Q. Or the researchers?</p> <p>23 A. Several of them, yes.</p> <p>24 Q. And it's my understanding</p>	<p style="text-align: right;">Page 296</p> <p>1 ovarian cancer and that asbestos and</p> <p>2 talcum powder were associated with an</p> <p>3 increased risk; is that correct?</p> <p>4 MS. SHARKO: Objection to</p> <p>5 form. Lacks foundation.</p> <p>6 THE WITNESS: There are</p> <p>7 several questions there. Can you</p> <p>8 break them up?</p> <p>9 BY DR. THOMPSON:</p> <p>10 Q. Okay. These authors</p> <p>11 included inflammation under behavioral</p> <p>12 and inflammatory risk factors, correct?</p> <p>13 A. I think that you have to</p> <p>14 understand how to read the scientific</p> <p>15 literature. "Suggests a possible</p> <p>16 association" is a very weak statement.</p> <p>17 That means they suggest. That doesn't</p> <p>18 mean they establish. "Suggests a</p> <p>19 possible association between inflammation</p> <p>20 and increased risk of ovarian cancer."</p> <p>21 So no, it's not as strong as</p> <p>22 you made it out to be Number one.</p> <p>23 Number two is I've read the</p> <p>24 Poole, et al., paper and I have read the</p>
<p style="text-align: right;">Page 295</p> <p>1 that the authors of this treatise</p> <p>2 included not only GYN oncologists, but</p> <p>3 epidemiologists, molecular biologists,</p> <p>4 and others so that it would be a</p> <p>5 comprehensive report.</p> <p>6 A. Yes.</p> <p>7 Q. Is that your understanding</p> <p>8 as well?</p> <p>9 A. Mm-hmm.</p> <p>10 MS. SHARKO: Object to the</p> <p>11 form.</p> <p>12 BY DR. THOMPSON:</p> <p>13 Q. And it was also meant to be</p> <p>14 a state of the science in ovarian cancer</p> <p>15 research treatise.</p> <p>16 And this was published in</p> <p>17 2016, I believe; is that right?</p> <p>18 A. I think so.</p> <p>19 MS. SHARKO: Object to the</p> <p>20 form.</p> <p>21 BY DR. THOMPSON:</p> <p>22 Q. So at least these</p> <p>23 researchers had the opinion that</p> <p>24 inflammation was a risk factor for</p>	<p style="text-align: right;">Page 297</p> <p>1 subsequent papers by Poole and others.</p> <p>2 And the association between inflammation</p> <p>3 and increased risk of ovarian cancer, it</p> <p>4 doesn't distinguish between whether the</p> <p>5 inflammation is a marker of existing</p> <p>6 ovarian cancer or the inflammation is a</p> <p>7 cause of cancer, which has been what we</p> <p>8 discussed all morning.</p> <p>9 So I don't really think that</p> <p>10 this statement is in any way</p> <p>11 contradictory to anything that I've said</p> <p>12 this morning.</p> <p>13 As to the statement about</p> <p>14 asbestos and ovarian cancer, I've already</p> <p>15 said that I don't really have an opinion.</p> <p>16 I haven't had time or wasn't charged with</p> <p>17 doing an extensive analysis of ovarian</p> <p>18 cancer and asbestos.</p> <p>19 So I really don't think that</p> <p>20 I should comment on this statement. But</p> <p>21 it doesn't really review the evidence.</p> <p>22 Just to be -- just to point out that this</p> <p>23 statement does not review the evidence,</p> <p>24 it simply cites previous conclusions. So</p>

<p style="text-align: right;">Page 298</p> <p>1 it really doesn't analyze the case any 2 more than those original papers did. 3 As for the statement of 4 talc, it cites, you know -- it cites two 5 studies that are, again, I think, both 6 case-control studies. It does not in any 7 way comprehensively review the 8 literature, and it says it's been 9 associated with it. It doesn't say it's 10 a causal association, which I thought was 11 what we were going to be discussing here 12 today. 13 DR. THOMPSON: I'll object 14 as nonresponsive. 15 BY DR. THOMPSON: 16 Q. Because my question was, did 17 these authors include a section on 18 inflammation in this treatise? 19 A. They -- they included a 20 section, but as I said, the section says 21 there's a possible association between 22 inflammation and an increased risk of 23 ovarian cancer. 24 Q. And if the authors didn't</p>	<p style="text-align: right;">Page 300</p> <p>1 There are a number of different 2 tumor types with characteristic 3 histologic features, distinctive 4 molecular signatures, and disease 5 trajectories." Moreover -- 6 MS. SHARKO: Slow. 7 THE WITNESS: "Moreover, 8 these tumors are heterogeneous and 9 they can arise from different 10 tissues of the female reproductive 11 tract." 12 So again, it just states 13 what I've been saying all day, is 14 that is that it's not meaningful 15 to talk about ovarian cancer as a 16 single entity. You have to break 17 it down into each of the diseases. 18 DR. THOMPSON: And that was 19 nonresponsive, because there was 20 not a question about asking 21 anything to do with that. 22 MS. SHARKO: Ignore that 23 comment and wait for the next 24 question.</p>
<p style="text-align: right;">Page 299</p> <p>1 think it was plausible that that 2 association would be there, would they 3 have included it? 4 A. I don't presume to be in the 5 mind of the authors, and I don't know 6 which of the authors was the major author 7 of this section. So I can't answer that 8 question to any degree of certainty. 9 Can I point out one other 10 thing? 11 Q. I don't -- there's not a 12 question on the table. 13 MS. SHARKO: No, he's 14 finishing his answer. 15 THE WITNESS: I didn't 16 finish. 17 DR. THOMPSON: No, he's not. 18 MS. O'DELL: He is not. 19 THE WITNESS: I am. I meant 20 to point out that on Page 9, the 21 same preface that you only read a 22 small part of, at the bottom says, 23 "An overarching conclusion is that 24 ovarian cancer is not one disease.</p>	<p style="text-align: right;">Page 301</p> <p>1 DR. THOMPSON: Object as 2 nonresponsive. 3 BY DR. THOMPSON: 4 Q. Did you -- Dr. Neel, did you 5 review the literature on pleurodesis? 6 A. Not extensively, no. 7 Q. Was it not relevant, the 8 reaction in the tissue caused by talc 9 injected into the pleural space to 10 treat -- 11 A. It's relevant for the study 12 of mesothelioma. 13 Q. But it's not relevant for 14 the study of the inflammatory effect of 15 talc in the body? 16 A. It would be potentially 17 relevant to the studies of peritoneal 18 mesothelioma. But it's not necessarily 19 relevant to ovarian cancer, no. 20 Q. So it's your testimony that 21 injection of talcum powder into the 22 pleural space has no meaning at all for 23 what the reaction might be in a tissue 24 like the ovary?</p>

Page 302	Page 304
<p>1 A. It has relevance to what --</p> <p>2 MR. LOCKE: Objection.</p> <p>3 THE WITNESS: Can I answer</p> <p>4 the question?</p> <p>5 MS. SHARKO: Yes.</p> <p>6 THE WITNESS: So it's --</p> <p>7 MS. SHARKO: You have to</p> <p>8 give everybody time to object.</p> <p>9 THE WITNESS: It has</p> <p>10 relevance to what the response of</p> <p>11 the mesothelial cells of the</p> <p>12 pleural cavity are. It might be</p> <p>13 somewhat relevant to the response</p> <p>14 of the pleural -- sorry the</p> <p>15 peritoneal mesothelial cells. But</p> <p>16 there are direct experiments that</p> <p>17 address, some of which we've</p> <p>18 discussed before, the effects of</p> <p>19 talc injections into the relevant</p> <p>20 tissues of ovarian cancer. So why</p> <p>21 would I look at the irrelevant</p> <p>22 tissues?</p> <p>23 BY DR. THOMPSON:</p> <p>24 Q. Because, do we have any</p>	<p>1 And also sort of the</p> <p>2 sentiment behind the FDA, and it's</p> <p>3 also what's listed on the NCI</p> <p>4 website.</p> <p>5 So I don't really think we</p> <p>6 should use the form -- the term</p> <p>7 "suggested carcinogen."</p> <p>8 That being said, no, it</p> <p>9 would not be ethical to do that</p> <p>10 study.</p> <p>11 BY DR. THOMPSON:</p> <p>12 Q. And if you had read that</p> <p>13 Health Canada assessment, you would know</p> <p>14 that Health Canada actually does suggest</p> <p>15 a causal association?</p> <p>16 MS. SHARKO: Object.</p> <p>17 MR. LOCKE: Objection.</p> <p>18 MS. SHARKO: Object to the</p> <p>19 form. Lacks foundation.</p> <p>20 Misstates the evidence.</p> <p>21 THE WITNESS: I'm happy to</p> <p>22 look over the thing and discuss it</p> <p>23 with you, but I did read the</p> <p>24 Taher, et al., paper, and the</p>
Page 303	Page 305
<p>1 studies of injecting talcum powder into a</p> <p>2 woman's ovaries?</p> <p>3 A. Into female -- into actual</p> <p>4 females?</p> <p>5 Q. Yes.</p> <p>6 A. Not that I'm aware of.</p> <p>7 Q. Would it be ethical to</p> <p>8 inject a suspected carcinogen into a</p> <p>9 woman's ovaries?</p> <p>10 A. Well, I --</p> <p>11 MS. SHARKO: Object to the</p> <p>12 form of the question. Lacks</p> <p>13 foundation.</p> <p>14 THE WITNESS: First of all,</p> <p>15 I categorically deny that it's a</p> <p>16 suspected carcinogen. It's</p> <p>17 characterized as a possible</p> <p>18 carcinogen. And that has been the</p> <p>19 standard -- that has been the</p> <p>20 conclusion, not just of IARC but</p> <p>21 also of the -- of the Taher, et</p> <p>22 al., report. So I assume that's</p> <p>23 what Health Canada will end up</p> <p>24 saying.</p>	<p>1 Taher, et al., paper says the</p> <p>2 same -- basically the same thing</p> <p>3 as IARC: Possible.</p> <p>4 BY DR. THOMPSON:</p> <p>5 Q. And -- I'll leave it at</p> <p>6 that.</p> <p>7 (Document marked for</p> <p>8 identification as Exhibit</p> <p>9 Neel-28.)</p> <p>10 DR. THOMPSON: I'm going to</p> <p>11 mark this next article as</p> <p>12 Exhibit 28. And I just -- oh, I</p> <p>13 do have two.</p> <p>14 MS. SHARKO: Thank you.</p> <p>15 BY DR. THOMPSON:</p> <p>16 Q. The correspondence that I'm</p> <p>17 interested in having you discuss with me</p> <p>18 is on the second page, "Talcum should not</p> <p>19 be used for pleurodesis with nonmalignant</p> <p>20 pleural effusions."</p> <p>21 And I'll give you a chance</p> <p>22 to look at that if you'd like.</p> <p>23 A. Yeah. So that is these</p> <p>24 people's opinion.</p>

<p style="text-align: right;">Page 306</p> <p>1 Q. I agree. But at least these 2 scientists felt strongly that talc should 3 not be used for pleurodesis, correct? 4 A. Apparently, yes. 5 Q. And they stated that "talc 6 is not a uniform substance and varies 7 significantly in size and chemical 8 composition with the latter depending on 9 geologic origin. This sheet silicate can 10 be contaminated with" -- "by asbestos, in 11 association between carcinogenesis and 12 exposure to asbestos included in talc, 13 appears credible." 14 Do you have an opinion 15 regarding that statement? 16 A. Yes. As I said, I think 17 that -- that my opinion, based on 18 everything that I've read is as I've 19 stated it in my report, which is that 20 there's no credible scientific evidence 21 that talc causes cancer in the female 22 genital tract. 23 So again, I don't really 24 think that this -- there's -- this is</p>	<p style="text-align: right;">Page 308</p> <p>1 A. That's what they said. But 2 I have nothing to say about that. As 3 I've said before. 4 Q. So you have no knowledge one 5 way or the other whether fibers occur in 6 talcum powder, and if so, whether there 7 would be any health hazard as a result? 8 A. I can only comment on the 9 studies that I read and commented on in 10 my report, which have to do with the use 11 of talc as cited in the methods and 12 materials sections of the epidemiology 13 studies and in the specific biological 14 experiments that I cited. 15 I am not a mineralogist. I 16 am not a geologist. I have no comment on 17 the composition of talc today or prior to 18 today, like in 2001, which was much long 19 ago. So I don't even know that it's 20 relevant to today. 21 Q. If you have a -- if you turn 22 to Page 25 of your report. And you are 23 discussing the Buz'Zard paper. And your 24 opinion is that "this study and its</p>
<p style="text-align: right;">Page 307</p> <p>1 basically just citing a couple of papers, 2 and it's not in any way reputing anything 3 that I've said, so... 4 And I don't even know where 5 it's from. It's not cited on there. It 6 wasn't -- I don't -- 7 Q. It's not -- it's from the 8 American Journal of Respiratory -- 9 A. Yeah. 10 Q. -- and Critical Care 11 Medicine, 2001. 12 A. Which, again, this was in 13 2001. There's a lot of science since 14 2001. I don't think it's relevant. 15 And furthermore it's not 16 peer reviewed. 17 So I don't think it's 18 relevant. 19 Q. And that's fine. But I am 20 still entitled to ask you about it. 21 The authors at least were 22 concerned about the presence of fibers, 23 talc fibers in talcum powder used for 24 pleurodesis, correct?</p>	<p style="text-align: right;">Page 309</p> <p>1 interpretation by plaintiffs' experts is 2 seriously flawed for multiple reasons." 3 The first reason that you 4 give is, "The -- "the talc was obtained 5 from a standard chemical reagent company, 6 Sigma, and its quality, mineral and/or 7 fibrous content and composition were not 8 assessed." 9 A. Mm-hmm. 10 Q. And that was a criticism of 11 the Buz'Zard paper, correct? 12 A. Yes. Correct. 13 Q. Do you know anything 14 whatsoever about the quality, mineral 15 and/or fibrous content and composition of 16 Johnson's Baby Powder? 17 A. No. But I know that -- that 18 this study just used Sigma talc. So it's 19 not directly relevant to Johnson & 20 Johnson's products. That was my point in 21 that statement. 22 Q. So studies done with talcum 23 powder would not be relevant to Johnson's 24 Baby Powder?</p>

<p style="text-align: right;">Page 310</p> <p>1 A. Studies done with talcum 2 powder would not be directly relevant to 3 Johnson' Baby Powder, but studies done 4 with Johnson & Johnson Baby Powder are 5 relevant. So...</p> <p>6 But in any event, this paper 7 is not conclusive in any way that talc is 8 pro-oncogenic.</p> <p>9 Q. I -- I didn't ask that 10 question. That's nonresponsive.</p> <p>11 I was just asking why it 12 mattered what the quality, mineral, 13 and/or fibrous content and composition 14 were in the paper using talcum powder by 15 Buz'Zard.</p> <p>16 MS. SHARKO: Is that -- 17 wait. Is that a question? Or is 18 that an explanation for why you 19 asked the question?</p> <p>20 BY DR. THOMPSON: 21 Q. Does it matter what the 22 quality, mineral and/or fibrous content 23 and composition of talcum powder is when 24 you're assessing its potential molecular</p>	<p style="text-align: right;">Page 312</p> <p>1 in this litigation.</p> <p>2 You said prior to this 3 litigation, didn't you?</p> <p>4 Q. I did.</p> <p>5 Did you look at Dr. Saed's 6 CV after being retained to testify in 7 this litigation?</p> <p>8 A. I -- I didn't look. I don't 9 recall if I looked at his complete -- I 10 think I did look at his CV in the context 11 of his report. But I also did a search 12 on PubMed for the relevant papers.</p> <p>13 Q. That was Exhibit 29. A 14 partial --</p> <p>15 (Document marked for 16 identification as Exhibit 17 Neel-29.)</p> <p>18 MS. SHARKO: This begins 19 with Page 29?</p> <p>20 DR. THOMPSON: Yes.</p> <p>21 MS. SHARKO: Is that 22 correct?</p> <p>23 DR. THOMPSON: Yes.</p> <p>24 BY DR. THOMPSON:</p>
<p style="text-align: right;">Page 311</p> <p>1 effects?</p> <p>2 MS. SHARKO: Objection. 3 Asked and answered.</p> <p>4 THE WITNESS: It matters if 5 you are trying to infer from 6 studies done with Sigma that that 7 definitely applies to Johnson & 8 Johnson's products.</p> <p>9 But in this case, because 10 the evidence doesn't really say 11 anything that's relevant, it 12 doesn't matter.</p> <p>13 BY DR. THOMPSON: 14 Q. You are very critical of 15 Dr. Saed's work, correct?</p> <p>16 A. Yes.</p> <p>17 Q. Did you look at Dr. Saed's 18 CV prior to this litigation?</p> <p>19 A. No.</p> <p>20 Q. Would that be something that 21 you would be interested in, as to what 22 Dr. Saed has published previously?</p> <p>23 A. Oh, I looked at his 24 publications subsequent to being engaged</p>	<p style="text-align: right;">Page 313</p> <p>1 Q. And like -- like yourself, 2 Dr. Saed's CV is quite extensive.</p> <p>3 A. I wouldn't agree with that 4 statement.</p> <p>5 Q. Okay. It's 100, over 100 6 pages. So --</p> <p>7 A. Quantity is not quality.</p> <p>8 Q. I --</p> <p>9 A. It's voluminous, but it's 10 not published in highly cited journals, 11 and I'm sure his H index is quite low.</p> <p>12 Q. I didn't ask any question 13 about where it was --</p> <p>14 A. Yes, you did.</p> <p>15 Q. -- where it was published 16 or -- I just --</p> <p>17 A. Well, that's quite relevant.</p> <p>18 MS. SHARKO: All right. 19 What's the next question?</p> <p>20 DR. THOMPSON: Well, if you 21 let me ask it, I will.</p> <p>22 MS. SHARKO: Thank you.</p> <p>23 BY DR. THOMPSON: 24 Q. Did you consider Dr. Saed's</p>

<p style="text-align: right;">Page 314</p> <p>1 CV important or Dr. Saed's previous 2 publications?</p> <p>3 A. Once I read them, yes. I 4 didn't read all of them. But I read 5 several of them, as I've cited in my 6 report. And I'm happy to go through each 7 one of them and show why they're all 8 flawed.</p> <p>9 Q. I'm asking questions.</p> <p>10 A. I'm answering your 11 questions.</p> <p>12 Q. That's not something I want 13 to know. I don't believe I asked that 14 particular question.</p> <p>15 A. You asked me if I considered 16 them relevant. And I told you that I 17 did. And I read them, and that's why I 18 assessed the studies as quite poor.</p> <p>19 Q. Looking at his CV, would you 20 agree that the focus of his lab has the 21 study of oxidative stress and its 22 biological effects?</p> <p>23 MS. SHARKO: We don't have 24 his CV in front of us.</p>	<p style="text-align: right;">Page 316</p> <p>1 epithelial ovarian cancer?</p> <p>2 A. I don't know what "many 3 scientists" mean. Some scientists do.</p> <p>4 Q. Some scientists?</p> <p>5 A. Yes.</p> <p>6 Q. Do you disagree with those 7 scientists?</p> <p>8 A. I think that oxidative 9 stress resulting from follicular fluid 10 that's released from ovarian -- from 11 ovulation events, there could be 12 prooxidant species in there. But I 13 certainly think that oxidative stress 14 arising from general metabolism, which is 15 primarily endogenous, mitochondrial 16 oxygen -- the act of oxygen production 17 can contribute to cancer generation.</p> <p>18 Q. And you do not believe that 19 oxidative stress from exogenous factors 20 plays a role?</p> <p>21 A. I don't think there's any 22 compelling evidence that oxidative stress 23 from exogenous agents plays a role in 24 high grade serous ovarian cancer. That's</p>
<p style="text-align: right;">Page 315</p> <p>1 BY DR. THOMPSON:</p> <p>2 Q. Looking at his published 3 articles, would you agree that the focus 4 of his lab has been the study of 5 oxidative stress and its biological 6 effects?</p> <p>7 A. Some of the papers are on 8 that. Some of them are on other things. 9 So, you know, one area of focus appears 10 to be on oxidative stress.</p> <p>11 Q. What is oxidative stress?</p> <p>12 A. So cells are exposed to -- 13 we live in an oxidative environment, as 14 we breathe oxygen. So we live in a 15 highly oxidative environment. And 16 proteins and other biomolecules, 17 including DNA, undergo oxidative events.</p> <p>18 And oxidative stress occurs 19 when the pro-oxidative potential of cells 20 exceeds the antioxidant capacity of 21 cells. So that's oxidative stress.</p> <p>22 Q. And is it fair to say that 23 many scientists believe that oxidative 24 stress plays a role in the etiology of</p>	<p style="text-align: right;">Page 317</p> <p>1 what I think.</p> <p>2 I think that it's 3 conceivable, one of the possible 4 mechanisms by which obesity promotes 5 other forms of ovarian cancer, is 6 through -- indirectly through oxidative 7 stress, and there are several mechanisms 8 for that.</p> <p>9 Q. Is a role that oxidative 10 stress plays in the pathogenesis of 11 cancer and ovarian cancer something that 12 would be considered controversial in the 13 scientific community, would you say?</p> <p>14 A. I think it's open to 15 question, yes. I think -- yes.</p> <p>16 Q. So there's some scientists 17 that believe that it does play a role and 18 others that believe -- who believe it 19 does not, correct?</p> <p>20 A. Yes, but talking about 21 oxidative stress, you have to realize 22 it's -- to be meaningful, you have to 23 really narrow down what kind of sources 24 of oxidative stress we are talking about.</p>

<p style="text-align: right;">Page 318</p> <p>1 Q. And is it your opinion that 2 oxidative stress from exogenous sources 3 has no role in ovarian cancer? 4 A. I think I just answered that 5 question. 6 Q. Okay. And do you believe 7 that the scientists that would take 8 another position are unreasonable? 9 A. I would have to see the 10 details of the position. My objection to 11 Dr. Saed's data, results or claims, are 12 not that he's taking another position. 13 It's that the evidence that he adduces to 14 support his claims is either nonexistent 15 or poor. 16 Q. But there are other 17 scientists that have reported similar 18 experiments and -- to Dr. Saed, and would 19 you include them in the same category? 20 A. You'll have to tell me 21 exactly what experiments you are 22 referring to. 23 Q. Okay. 24 A. I don't think anybody has</p>	<p style="text-align: right;">Page 320</p> <p>1 as nonresponsive. 2 BY DR. THOMPSON: 3 Q. I asked you for a paper. 4 A. Well, the paper -- the paper 5 is the TCGA report. And if you look at 6 the tables that come with the TCGA report 7 which are now put on websites, and it is 8 there. So yes, the TCGA 2012 report has 9 RNA sequencing data on ovarian cancers, 10 and if you look at that you will see that 11 there's no significant expression of 12 myeloperoxidase in ovarian cancer. 13 MS. SHARKO: Mr. Tisi, could 14 you -- it's happened several 15 times. Could you please not talk 16 while the witness is talking. 17 MR. TISI: Actually I don't 18 think -- I'd be curious if you 19 heard it. 20 THE WITNESS: I actually 21 did, but I tried to focus on DR. 22 THOMPSON. 23 MR. TISI: I'm allowed to 24 whisper to my colleague here. So</p>
<p style="text-align: right;">Page 319</p> <p>1 reported the myeloperoxidase in ovarian 2 cancer cells because it doesn't appear to 3 be. So there's many statements, as I 4 pointed out in my report, that are 5 contradicted by other data in the 6 literature, including large scale studies 7 done by international groups to look at 8 ovarian cancer genetics. 9 Q. Can you direct me to a paper 10 that explicitly states that 11 myeloperoxidase does not occur in ovarian 12 cancer cells? 13 A. If you look on the website 14 that has all of the RNA sequencing data 15 from the TCGA, you can see as I showed 16 you in my report, that the level of 17 myeloperoxidase RNAs below the level of 18 action of tumor suppressing gene. So 19 that is data. 20 If you would like to look 21 through the tables of the TCGA report on 22 which that's based, you can find the 23 actual RNA sequence for myeloperoxidase. 24 DR. THOMPSON: Not -- object</p>	<p style="text-align: right;">Page 321</p> <p>1 if I interrupt you, I apologize. 2 Would you do me a favor and let me 3 know if -- 4 MS. SHARKO: No. His job 5 is -- his job is not to police 6 you, Mr. Tisi. 7 MR. TISI: Well, your job is 8 not to -- is not to school me, 9 Susan. So I apologize if he heard 10 me. And I leaned over and spoke 11 to my colleague here. So please 12 proceed. 13 DR. THOMPSON: We're going 14 to look at some of Dr. Saed's 15 other literature. 16 BY DR. THOMPSON: 17 Q. But I think there are 18 several papers regarding myeloperoxidase. 19 Those have all been peer-reviewed, the 20 ones that are published, correct? 21 MS. SHARKO: I object to the 22 form of the question. 23 BY DR. THOMPSON: 24 Q. Has Dr. Saed published</p>

<p style="text-align: right;">Page 322</p> <p>1 papers regarding myeloperoxidase that 2 have been peer-reviewed? 3 A. Yes, he has. 4 Q. And there are other authors 5 on those papers as well, correct? 6 A. I think they are all from 7 his lab. 8 Q. Is there any overlap between 9 your research and phosphorylation 10 cascades and signal transduction -- did 11 I -- was that kind of close? 12 A. It's good. 13 Q. It worked. All right. 14 -- and Dr. Saed's research 15 in oxidative stress? 16 A. I'm an expert in oxidation 17 of protein-tyrosine phosphatases. We 18 developed some of the novel technologies 19 that were published in high quality 20 journals on this subject. So I do have, 21 you know, a significant familiarity with 22 the issues attended to oxidative stress 23 and oxidation-induced signaling. 24 So ox -- you know, reactive</p>	<p style="text-align: right;">Page 324</p> <p>1 exclusive -- 2 A. I don't -- 3 Q. -- to what you're working 4 on? 5 A. I know -- so my interest in 6 oxidation has to do with normal 7 physiological regulation and pathological 8 regulation of protein tyrosine 9 phosphatase activity. 10 I'm not sure which 11 particular paper of Dr. Saed you are 12 referring to, but I think many of the 13 papers don't address what you say they 14 are addressing. They may say that in the 15 title, but they don't address that issue. 16 Q. You would agree that 17 inflammation is part of a wider signaling 18 network, wouldn't you? 19 A. That inflammation is part of 20 a wider signaling network? No, I 21 wouldn't agree with that statement. I 22 don't see that that's-- 23 Q. Is -- is -- 24 A. -- it's a non sequitur in my</p>
<p style="text-align: right;">Page 323</p> <p>1 oxygen species are not just produced as a 2 pathological event. They're actually 3 part of normal growth factor and cytokine 4 signaling. And I've worked on the fact 5 that oxidative -- reactive oxygen species 6 react with the highly activated 7 neutrophilic cysteines, neutrophilic 8 cysteines of protein-tyrosine 9 phosphatases. And that's thought to be 10 part of normal signaling. That's the 11 only overlap. 12 Q. And I understand that you do 13 not accept Dr. Saed's research as 14 credible. But I'm trying to establish if 15 your work and his work are mutually 16 exclusive. Can both -- can -- are both 17 plausible mechanisms? 18 A. My work -- my -- well, you 19 haven't told me what mechanisms of 20 Dr. Saed you are talking about. 21 Q. Well, let's just say 22 oxidative stress and its role in the 23 pathogenesis of ovarian cancer. 24 Is that mutually</p>	<p style="text-align: right;">Page 325</p> <p>1 opinion. 2 Q. Is oxidative stress a part 3 of a wider signaling network in your 4 opinion? 5 A. What do you mean by 6 signaling network? I mean you're using, 7 you know, jargon that's not very 8 specific. 9 Q. Well, I probably read that 10 somewhere. 11 Are there researchers -- I'm 12 thinking particularly of Dr. Finkel? Do 13 you know Dr. Finkel? 14 A. Torin Finkel? Yes, I 15 know -- I don't know Torin Finkel 16 personally, but I know his work. 17 Q. Does Dr. Finkel study signal 18 transduction by reactive oxygen species? 19 A. Yes. His initial studies 20 were the ones that provided the first 21 evidence that normal react -- that 22 reactive oxygen species were produced in 23 response to normal growth factor 24 signaling. I think the original paper</p>

<p style="text-align: right;">Page 326</p> <p>1 was on PDGF stimulation of smooth muscle 2 cells and the evidence was that blocking 3 oxidate with hydrogen peroxide generation 4 by smooth muscle cells impeded PDGF 5 receptor phosphorylation, which actually 6 got me interested in the field since the 7 most plausible mechanism by which that 8 might occur would be inhibition of 9 tyrosine phosphatase which we were 10 working on -- we and others subsequently 11 provided evidence to support that, as did 12 Finkel.</p> <p>13 Q. And that would be intrinsic 14 ROS?</p> <p>15 A. That would be --</p> <p>16 Q. Or --</p> <p>17 A. -- those would be -- that 18 would be intrinsically produced ROS in 19 response to growth factor signaling, not 20 through mitochondria probably, but 21 through a series of enzymes called NOXs 22 or NADPH oxidases.</p> <p>23 Q. Do you agree that an 24 increase in ROS levels under certain</p>	<p style="text-align: right;">Page 328</p> <p>1 regarding oxidative stress and ovarian 2 cancer, correct?</p> <p>3 MS. SHARKO: Wait. I -- I 4 object to the preface and the 5 speech and, therefore, the form of 6 the question.</p> <p>7 What is the question you're 8 asking him?</p> <p>9 BY DR. THOMPSON:</p> <p>10 Q. Dr. Saed does not have 427 11 publications on oxidative stress and 12 cancer, does he?</p> <p>13 A. Well, I don't think he has 14 427 publications. So I guess that means 15 he doesn't have 427 publications on 16 oxidative stress and cancer.</p> <p>17 Q. So someone else is 18 publishing on oxidative stress and 19 ovarian cancer, correct?</p> <p>20 A. I don't know. I haven't 21 done the specific search you did and I 22 haven't looked at the papers but I'm 23 happy to look at every single one of 24 them.</p>
<p style="text-align: right;">Page 327</p> <p>1 conditions can cause DNA mutations?</p> <p>2 A. Yes.</p> <p>3 Q. And cancer is the result of 4 genetic mutations, correct?</p> <p>5 A. Yes.</p> <p>6 Q. So under the right 7 conditions, chronic inflammation could 8 result in increasing ROS that could cause 9 genetic mutations that could cause 10 cancer, theoretically?</p> <p>11 A. In certain context, yes.</p> <p>12 Q. When I searched PubMed, I 13 found the following, searching cancer and 14 inflammation. 78,901, does that sound 15 reasonable?</p> <p>16 A. I have no idea, but I 17 wouldn't --</p> <p>18 Q. Ovarian cancer and 19 inflammation, 1306. Oxidative stress and 20 cancer, 23,845 publications. And 21 oxidative stress and oxidative cancer, 22 427.</p> <p>23 Dr. Saed doesn't have 24 anywhere close to 427 publications</p>	<p style="text-align: right;">Page 329</p> <p>1 And I'm not saying that 2 there is no possibility that oxidative 3 stress plays a role in ovarian cancer. 4 I'm saying Dr. Saed's papers are 5 categorically and fundamentally flawed in 6 almost every single instance.</p> <p>7 Q. So are you saying that 8 oxidative stress is a plausible mechanism 9 for ovarian cancer?</p> <p>10 A. I'm not taking a position 11 one way or the other on that issue.</p> <p>12 Q. Okay. So you do not have 13 a -- you don't have a position on whether 14 oxidative stress has a role in the 15 pathogenesis of ovarian cancer. Your 16 opinions today are specifically about 17 Dr. Saed and his work?</p> <p>18 MS. SHARKO: Object to the 19 form of the question. Lacks 20 foundation.</p> <p>21 THE WITNESS: Can you ask 22 both questions separately?</p> <p>23 BY DR. THOMPSON:</p> <p>24 Q. Yeah.</p>

<p style="text-align: right;">Page 330</p> <p>1 A. I categorically say that 2 none of Dr. Saed's work that was put 3 forward as evidence in support of his 4 contentions in his report is credible. 5 That I say categorically. 6 Q. Okay. 7 A. In terms of whether 8 oxidative stress plays a role in ovarian 9 cancer, that question is too broad. If 10 you narrow the question and ask me a more 11 specific question, I might be able to 12 give an opinion. But I think the issue 13 is still under debate. 14 I think I made it very clear 15 what the well-established pathogenesis of 16 ovarian cancer is. 17 There's -- there is one SNP 18 which I mentioned in my report, GPX-6, 19 which interestingly is not a SNP that 20 Dr. Saed cites, because I don't think 21 he's familiar with the GWAS literature. 22 That's the -- is associated. 23 I haven't had a chance to 24 really look in detail as to what's known</p>	<p style="text-align: right;">Page 332</p> <p>1 for publication. 2 But if you'd like me to look 3 at the final paper, I'm happy to do it. 4 I doubt that there's anything 5 different -- that's materially different 6 from what I wrote in my report. 7 Q. But you didn't see any 8 reason to look at it? 9 A. I didn't realize it was out 10 yet. 11 Q. And your attorneys didn't 12 provide the final published paper? 13 A. They mentioned to me 14 yesterday that the -- 15 MS. SHARKO: Well, wait, 16 wait. What was discussed with the 17 attorneys is privileged. 18 BY DR. THOMPSON: 19 Q. In your report you state 20 that Dr. Saed's work is "technically and 21 conceptually flawed and does not 22 withstand critical scrutiny." 23 Did you write that 24 statement?</p>
<p style="text-align: right;">Page 331</p> <p>1 about that SNP. So that SNP does raise 2 the possibility that oxidative stress in 3 some form might be involved in the 4 pathogenesis of some ovarian cancer. But 5 I haven't really studied that in detail. 6 BY DR. THOMPSON: 7 Q. In -- in your -- you have 8 not seen Dr. Saed's published paper, 9 correct? 10 A. I saw the manuscript that 11 was accepted for publication. 12 Q. But you don't know whether 13 that manuscript is the same as what was 14 actually published, correct? 15 A. Manuscripts accepted for the 16 publication in my 30 years of experience 17 as a faculty member are identical, except 18 for minor positioning of figures. 19 Q. Okay. So you've never made 20 edits on the final proof that's come back 21 to you? 22 A. If it's accepted for 23 publication, that's the final proof. 24 The -- the version that's marked accepted</p>	<p style="text-align: right;">Page 333</p> <p>1 A. Yes. Every word. 2 Q. Is that a statement that you 3 would put in a scholarly publication? 4 A. Technically and conceptually 5 flawed, yes. But it would be assumed if 6 I said that paper was -- in fact I've 7 used that phrase many times in reviews. 8 Well, sometimes I say technically flawed. 9 Sometimes I say conceptually flawed. And 10 when, as in the case of Dr. Saed's work, 11 it's both, I say conceptually and 12 technically flawed. That's exactly the 13 wording that I would use in reviews. 14 That being said, I would not 15 say that it wouldn't withstand scientific 16 scrutiny because it would be assumed and 17 understood by all scientists, including 18 editors of journals, that when I say 19 those statements that it doesn't 20 withstand scientific scrutiny. 21 Q. That paper was peer-reviewed 22 and accepted for publication and 23 published, correct? 24 A. At a very low impact</p>

<p style="text-align: right;">Page 334</p> <p>1 journal, yes.</p> <p>2 Q. And did you review the peer</p> <p>3 reviewers' comments to Dr. Saed's paper?</p> <p>4 A. I did. I think I cited some</p> <p>5 of the peer reviewers' comments.</p> <p>6 Q. And we'll go over those in a</p> <p>7 minute.</p> <p>8 And did you also write the</p> <p>9 sentence that questioned Dr. Saed's,</p> <p>10 quote, knowledge of basic cancer cell</p> <p>11 biology, genetics and biochemistry?</p> <p>12 A. Yes, I did.</p> <p>13 Q. What was your basis of</p> <p>14 questioning his knowledge of basic cancer</p> <p>15 cell biology, genetics and biochemistry?</p> <p>16 A. Well, there were several</p> <p>17 reasons that I based that. So it had to</p> <p>18 do with the fact that, for example, he</p> <p>19 mischaracterized -- can we go to the</p> <p>20 actual page in my report? I think I</p> <p>21 actually provide the explanations there.</p> <p>22 Where is that exactly? Oh, okay here. I</p> <p>23 said it.</p> <p>24 Q. Page 23.</p>	<p style="text-align: right;">Page 336</p> <p>1 there?</p> <p>2 A. I don't know what</p> <p>3 literature -- p53 is the paradigmatic</p> <p>4 tumor suppressor gene along with RD and</p> <p>5 PTEN.</p> <p>6 Q. And you state one of your</p> <p>7 basis for that claim is that Dr. Saed</p> <p>8 makes a truly extraordinary claim that</p> <p>9 talc treatment was associated with a</p> <p>10 genotype switch for SNPs in redox</p> <p>11 enzymes. If you read his paper, it would</p> <p>12 be clear that he was talking about a</p> <p>13 nucleotide -- nucleotide switch, correct?</p> <p>14 A. That's what a genotype is.</p> <p>15 MR. LOCKE: Objection.</p> <p>16 BY DR. THOMPSON:</p> <p>17 Q. Well, why is that an</p> <p>18 extraordinary claim?</p> <p>19 A. Because it's impossible that</p> <p>20 that would happen in 72 hours in, in</p> <p>21 effect, a single nucleotide with</p> <p>22 100 percent penetrance.</p> <p>23 Q. So do you believe that</p> <p>24 Dr. Saed made up his results?</p>
<p style="text-align: right;">Page 335</p> <p>1 A. Yes. Dr. Saed -- okay. For</p> <p>2 example, he states that p53 is an</p> <p>3 oncogene, whereas it is a paradigmatic</p> <p>4 tumor suppressor gene.</p> <p>5 He stated in his deposition</p> <p>6 that cells are grown at normal oxygen and</p> <p>7 glucose level.</p> <p>8 Q. And they --</p> <p>9 A. That's not true. I put the</p> <p>10 explanation.</p> <p>11 Q. I know. We're going to go</p> <p>12 over those now.</p> <p>13 A. I'm just answering your</p> <p>14 question.</p> <p>15 Q. For example, he states that</p> <p>16 p53 is an oncogene. Are you aware of</p> <p>17 literature that describes p53 as an</p> <p>18 oncogene?</p> <p>19 A. The lit -- p53 was</p> <p>20 originally described as an oncogene, and</p> <p>21 that was discovered subsequently that it</p> <p>22 was a tumor suppressor gene.</p> <p>23 Q. There is literature still</p> <p>24 that refers to p53 as an oncogene, isn't</p>	<p style="text-align: right;">Page 337</p> <p>1 A. I have no idea why Dr. Saed</p> <p>2 is making that claim. But it's simply</p> <p>3 impossible. It would be like finding a</p> <p>4 needle in a haystack and turning the</p> <p>5 needle into a hammer.</p> <p>6 Q. Did any of the peer</p> <p>7 reviewers say that that claim was</p> <p>8 extraordinary?</p> <p>9 A. I don't recall if they</p> <p>10 commented on it. I don't think they did,</p> <p>11 which illustrates the poor quality for</p> <p>12 peer review for that journal. There's no</p> <p>13 way that statement would have escaped the</p> <p>14 attention of any qualified peer reviewer.</p> <p>15 And I believe that if you</p> <p>16 read Dr. Birrer's report, he points to</p> <p>17 the same issue. So any qualified</p> <p>18 molecular biologist would have noted that</p> <p>19 and pointed out how absurd the claim.</p> <p>20 Q. Are you aware that the</p> <p>21 abstract that describes the mutations in</p> <p>22 the SNPs was reviewed by five to six</p> <p>23 reviewers and accepted for presentation</p> <p>24 at the SGO meeting?</p>

<p style="text-align: right;">Page 338</p> <p>1 A. I have no idea who reviewed 2 those. But they also have no knowledge 3 of modern molecular biology if they 4 accepted that claim. The fact that they 5 don't understand what they're reviewing 6 doesn't mean that they know what they're 7 talking about. I'm telling you that 8 there is absolutely no way that you can 9 get that kind of a genotype. 10 In -- plus, I looked at the 11 underlying data on which he based his 12 claim, and the actual assay is flawed, 13 and he didn't do the follow-up study that 14 would have been necessary to prove that 15 it was true. 16 MS. SHARKO: I would just 17 ask that we be provided with a 18 copy of these five to six peer 19 reviewers. I think the court 20 ordered you to do that, and I'll 21 send you yet another letter on it. 22 But that doesn't sound like 23 something that was produced to us 24 among the peer review that was.</p>	<p style="text-align: right;">Page 340</p> <p>1 question. 2 Since, you know, Ms. Sharko 3 challenged me, you've been program 4 director for meetings, correct? 5 A. Yes. 6 Q. What was your policy or AACR 7 policy for evaluating and determining 8 what abstracts to accept for presentation 9 at a meeting, at a national meeting? 10 A. First of all, my 11 understanding was that this was not 12 presented. It was presented as a poster. 13 That's a big difference. 14 Q. Okay. Whatever the level, 15 poster, presentation, published abstract. 16 How did that process work when were you 17 program director? 18 A. So we had people reviewing 19 the abstracts. The reviews for 20 abstracts, especially those for poster -- 21 when you review abstracts at a meeting 22 like this, there's literally thousands of 23 abstracts. So you have to read through a 24 lot of them very quickly. And the</p>
<p style="text-align: right;">Page 339</p> <p>1 And so, we'd like a copy. 2 DR. THOMPSON: There is 3 nothing in writing for abstracts 4 accepted for meetings. But I can 5 give you the policy of the meeting 6 regarding how abstracts are peer 7 reviewed. 8 MS. SHARKO: You just said 9 there were five to six peer 10 reviewers. Now you're saying 11 there aren't? 12 DR. THOMPSON: I said they 13 don't provide anything to the 14 authors of abstracts regarding the 15 results of their peer review. 16 THE WITNESS: Can I respond 17 to that? 18 BY DR. THOMPSON: 19 Q. I haven't asked you a 20 question. 21 MS. SHARKO: She's not going 22 to ask you the question. Sorry. 23 BY DR. THOMPSON: 24 Q. Sure. I'll ask you the</p>	<p style="text-align: right;">Page 341</p> <p>1 standard for accepting things for posters 2 is quite low. It's nowhere near rigorous 3 as what you would get for a high quality 4 journal. 5 And Basically, people just 6 want to see what's in the poster. 7 So the fact that it was 8 passed -- that five people looked at it 9 means that it was probably written in 10 English, and not much more. 11 Q. And if SGO accepts 12 25 percent of abstracts submitted, that 13 would probably be typical for a large 14 national meeting? 15 A. No. Not for posters. I 16 think when I was AACR program director, 17 we accepted a lot more than that. And 18 from other meetings, like Cold Spring 19 Harbor meetings and facet (ph) meetings, 20 we accept all the poster abstracts. It's 21 the presented ones, the ones that are 22 plenary sessions that are given as oral 23 presentations, those are the ones that 24 get a little bit more rigor.</p>

<p style="text-align: right;">Page 342</p> <p>1 And even there, that's not 2 really peer review. All we're seeing is 3 what the person provided in the abstract. 4 We're not seeing the data. And I'm 5 telling you from looking at the data, 6 it's an extraordinary claim. 7 Q. If SGO accepts 25 percent of 8 abstracts for any type of presentation, 9 whether it be poster or meeting, do you 10 have any reason to doubt that figure? 11 MS. SHARKO: Well, I object 12 to the form of the question. 13 Lacks foundation. And I'm not 14 sure I understand it. 15 THE WITNESS: So -- 16 BY DR. THOMPSON: 17 Q. Did you understand the 18 question? 19 A. Not really. What's the 20 question? 21 DR. THOMPSON: Okay. You 22 can leave off the speaking 23 objections. 24 BY DR. THOMPSON:</p>	<p style="text-align: right;">Page 344</p> <p>1 retained? 2 A. No. 3 Q. Did Dr. Saed publish 4 articles regarding cancer biology prior 5 to 2017? 6 A. Yes. Apparently. I mean, 7 from his CV and from my backwards search 8 of his record. 9 Q. And did Dr. Saed publish 10 articles about inflammation and ovarian 11 cancer prior to 2017? 12 A. He published papers that 13 claim to be about inflammation, yes. 14 That's not the same thing. 15 Q. It's not the same -- 16 A. We'd have to go through each 17 paper. 18 Q. -- thing to claim and to be 19 about inflammation? 20 A. Well, we'd have to go 21 through the actual paper to see whether 22 it's convincing. 23 For example, he says he 24 publishes papers about oxidative stress,</p>
<p style="text-align: right;">Page 343</p> <p>1 Q. The question is if SGO 2 represents that they accept 25 percent of 3 abstracts submitted at any level, do you 4 have any reason to dispute that? 5 A. I have no knowledge one way 6 or the other. I have no opinion on that 7 subject. 8 Q. Okay. And if SGO sends 9 abstracts to reviewers who identify 10 themselves as experts in the field, do 11 you have any reason to dispute that 12 representation? 13 A. I don't know what field 14 we're talking about. 15 Q. Molecular biology for 16 example? 17 MS. SHARKO: Object to the 18 form. Lacks foundation. 19 THE WITNESS: I have -- I 20 have no knowledge of what SGO 21 does. I don't go to SGO meetings. 22 BY DR. THOMPSON: 23 Q. Okay. Were you familiar 24 with Dr. Saed's work prior to being</p>	<p style="text-align: right;">Page 345</p> <p>1 but the papers just look at levels of 2 redox enzymes. And that alone does not 3 say anything about the net oxidative tone 4 in cells. You actually have to directly 5 measure it. 6 And as I said in my report, 7 he made these claims in his most recent 8 paper, which was just apparently 9 published, about oxidative stress. But 10 he never measured it. 11 So you can't really say that 12 there's a change in oxidative stress 13 without measurement. You actually have 14 to measure it. 15 He didn't measure 8-oxodG. 16 He didn't measure BODIPY. And he didn't 17 measure DCF florescence. Those are the 18 standard measurements, among others, for 19 looking at the net tone of reactive 20 oxygen species inside cells, or other 21 forms of reactive oxygen -- of -- of 22 oxidative stress like lipid peroxidation 23 or oxidative damage to DNA. 24 DR. THOMPSON: Object as</p>

<p style="text-align: right;">Page 346</p> <p>1 nonresponsive.</p> <p>2 BY DR. THOMPSON:</p> <p>3 Q. Did he publish any articles</p> <p>4 about ovarian cancer and oxidative stress</p> <p>5 prior to 2017?</p> <p>6 A. He did. And some of those</p> <p>7 are among the most that are off -- the</p> <p>8 most off point for this particular</p> <p>9 question.</p> <p>10 Q. Are you finished?</p> <p>11 A. Mm-hmm.</p> <p>12 Q. Did you review any of</p> <p>13 Dr. Saed's pre-2017 articles?</p> <p>14 A. Several of them, yes.</p> <p>15 Q. And did you bring those with</p> <p>16 you today?</p> <p>17 A. As I told you at the</p> <p>18 beginning of the deposition, I didn't</p> <p>19 bring anything with me today except my</p> <p>20 coat.</p> <p>21 Q. Are they listed on your</p> <p>22 materials considered list?</p> <p>23 A. Anything that I read of</p> <p>24 Dr. Saed's that I believe is relevant to</p>	<p style="text-align: right;">Page 348</p> <p>1 journals, including use of multiple</p> <p>2 siRNAs and rescue controls.</p> <p>3 So those -- those papers --</p> <p>4 which I'm absolutely sure I did cite</p> <p>5 somewhere in this report, or at least I'm</p> <p>6 pretty sure. We can go through my entire</p> <p>7 report, but I'm pretty sure that I cited</p> <p>8 those papers and that specific</p> <p>9 information, that that gives me -- that</p> <p>10 makes me question the quality of his</p> <p>11 work. As I said in my report.</p> <p>12 Q. But those papers were all</p> <p>13 peer reviewed and published in journals,</p> <p>14 correct?</p> <p>15 A. As I said, none of his</p> <p>16 papers are published in high -- in high</p> <p>17 impact journals and the quality of review</p> <p>18 at lower quality journals often matches</p> <p>19 the quality of the journal.</p> <p>20 Q. And you would consider</p> <p>21 Gynecologic Oncology a lower tiered</p> <p>22 journal?</p> <p>23 A. I think it depends on what's</p> <p>24 being published in Gynecological</p>
<p style="text-align: right;">Page 347</p> <p>1 this is referenced in thein the report.</p> <p>2 Q. I did not see any articles</p> <p>3 of Dr. Saed's listed.</p> <p>4 A. Then I didn't think they</p> <p>5 were relevant to the report.</p> <p>6 Q. So you do not think any of</p> <p>7 Dr. Saed's prior publications were</p> <p>8 relevant to your opinion that Dr. Saed</p> <p>9 lacks knowledge of basic cancer cell</p> <p>10 biology, genetics and biochemistry?</p> <p>11 A. No, I actually do think they</p> <p>12 were. I think -- I'm pretty sure I cited</p> <p>13 an earlier paper where he used -- where</p> <p>14 he did -- where -- for example, where he</p> <p>15 claimed that myeloperoxidase was in</p> <p>16 cells. He did that based on immuno</p> <p>17 staining, but he didn't have the proper</p> <p>18 controls for myeloperoxidase. So all he</p> <p>19 did was use an antibody. So that doesn't</p> <p>20 prove that it's there.</p> <p>21 And -- and his claims for</p> <p>22 perturbation experiments involve the use</p> <p>23 of siRNAs. And he didn't have the proper</p> <p>24 controls that are required by all major</p>	<p style="text-align: right;">Page 349</p> <p>1 Oncology. There are very fine papers</p> <p>2 published in Gynecological Oncology, but</p> <p>3 it depends on the particular topic.</p> <p>4 And high quality molecular</p> <p>5 biology papers are rarely published in</p> <p>6 Gynecologic Oncology. Some of them are.</p> <p>7 Q. How about Cancer?</p> <p>8 A. Cancer is a very low</p> <p>9 quality -- a low impact journal.</p> <p>10 Q. Would it be important for</p> <p>11 you to -- to look at the methodology that</p> <p>12 Dr. Saed had previously published in</p> <p>13 papers?</p> <p>14 A. As I just said, I did look</p> <p>15 at the methodology. I always read papers</p> <p>16 very extensively. When I -- I mean, one</p> <p>17 of the things that I focus on most is the</p> <p>18 methods.</p> <p>19 I always teach my students</p> <p>20 and postdocs that the methods are the</p> <p>21 most important thing you can read when</p> <p>22 evaluating a paper, because otherwise you</p> <p>23 can't know whether the data are valid.</p> <p>24 So, yes, I did extensively</p>

<p style="text-align: right;">Page 350</p> <p>1 look at his work.</p> <p>2 Q. And you'll agree that</p> <p>3 Dr. Saed has considered the molecular</p> <p>4 changes in various histologic subtypes of</p> <p>5 ovarian cancer, right?</p> <p>6 A. What do you mean considered?</p> <p>7 Q. He's published use --</p> <p>8 using -- looking at molecular changes in</p> <p>9 histologic subtypes?</p> <p>10 A. I'm not sure which paper you</p> <p>11 are referring to, but I don't really</p> <p>12 think so.</p> <p>13 In fact, one of the features</p> <p>14 of Dr. Saed's work is he does not appear</p> <p>15 to be aware of the recent evidence from</p> <p>16 Domcke, et al. and others that</p> <p>17 traditional so-called ovarian cancer cell</p> <p>18 lines are not representative of ovarian</p> <p>19 cancer -- at least traditional serous</p> <p>20 ovarian cancer cell lines are not really</p> <p>21 serous cancer lines.</p> <p>22 So he uses standard ovarian</p> <p>23 cancer cell lines in some of his work</p> <p>24 subsequent to the publication of his work</p>	<p style="text-align: right;">Page 352</p> <p>1 a break.</p> <p>2 THE VIDEOGRAPHER: Remove</p> <p>3 your microphones, please. The</p> <p>4 time is 3:34 p.m. Off the record.</p> <p>5 (Short break.)</p> <p>6 THE VIDEOGRAPHER: We are</p> <p>7 back on the record. The time is</p> <p>8 3:58 p.m.</p> <p>9 BY DR. THOMPSON:</p> <p>10 Q. Dr. Neel, are all the</p> <p>11 criticisms that you have of Dr. Saed</p> <p>12 contained in your report?</p> <p>13 A. I believe so, yes.</p> <p>14 Q. Are there --</p> <p>15 A. Of the papers that are</p> <p>16 relevant to this case, yes.</p> <p>17 Q. And are all the papers that</p> <p>18 you relied upon for your criticisms with</p> <p>19 Dr. Saed contained in the report?</p> <p>20 A. I believe so, I'd have to --</p> <p>21 can I look through the references? I'm</p> <p>22 pretty sure, but -- I guess his new</p> <p>23 paper, I don't have the final citation</p> <p>24 for that. So that would not be in the</p>
<p style="text-align: right;">Page 351</p> <p>1 such as Domcke, et al. in Nature</p> <p>2 Communications in 2013 that are not real</p> <p>3 serous cancer lines and yet he makes the</p> <p>4 claim that they are -- or he assumes that</p> <p>5 they are.</p> <p>6 So I did read those papers</p> <p>7 quite thoroughly. And I can tell you on</p> <p>8 multiple occasions his work is not</p> <p>9 scientifically conclusive and in some</p> <p>10 places categorically flawed.</p> <p>11 Q. Has Dr. Saed to your</p> <p>12 knowledge ever been reprimanded or</p> <p>13 sanctioned for publishing false data?</p> <p>14 A. I'm not accusing Dr. Saed of</p> <p>15 publishing false data. I'm accusing him</p> <p>16 of publishing bad science. I'm not</p> <p>17 accusing him of fraud. You only get</p> <p>18 reprimanded for fraud. Bad science, you</p> <p>19 just get a bad reputation.</p> <p>20 Q. Does Dr. Saed have a bad</p> <p>21 reputation?</p> <p>22 A. I don't know. But he does</p> <p>23 with me.</p> <p>24 DR. THOMPSON: Good time for</p>	<p style="text-align: right;">Page 353</p> <p>1 report.</p> <p>2 Let's see. I'd have to look</p> <p>3 through the report. If you want me to</p> <p>4 take the time, I'm happy to do it.</p> <p>5 Q. That's fine, because I need</p> <p>6 to know what literature you're relying on</p> <p>7 that forms the basis of your criticism of</p> <p>8 Dr. Saed.</p> <p>9 A. So I did read the paper. On</p> <p>10 Page 17, the statement that he made on</p> <p>11 his report on Page 5, ovarian cancer</p> <p>12 patients manifest significant -- because</p> <p>13 some of those refer to earlier papers,</p> <p>14 which I just read. But I just cited his</p> <p>15 statement in the report and pointed out</p> <p>16 that it wasn't really relevant to his</p> <p>17 contention for the purpose of this</p> <p>18 litigation. So I would have to go back</p> <p>19 and see what those papers were.</p> <p>20 Q. Where are you referring to?</p> <p>21 A. Page 17.A at the bottom.</p> <p>22 MS. SHARKO: We also served</p> <p>23 a supplemental materials</p> <p>24 considered list last night, DR.</p>

Page 354	Page 356
<p>1 THOMPSON. I assume you have that.</p> <p>2 DR. THOMPSON: Actually, I</p> <p>3 intended to mark that. I don't --</p> <p>4 THE WITNESS: Yeah. The</p> <p>5 same thing refers -- I'm sorry. I</p> <p>6 didn't want -- the same thing</p> <p>7 refers to Point B on Page 17.</p> <p>8 That refers to an earlier paper by</p> <p>9 Dr. Saed, which I just cited based</p> <p>10 on his report. And his earlier</p> <p>11 studies of -- the statements that</p> <p>12 he made about the SNPs. So all of</p> <p>13 those earlier papers on SNPs that</p> <p>14 are not confirmed by the GWAS,</p> <p>15 genomewide association studies to</p> <p>16 be relevant to ovarian cancer, and</p> <p>17 are listed here.</p> <p>18 So I -- so I based it on his</p> <p>19 report, and then I looked up the</p> <p>20 actual SNPs to see whether what he</p> <p>21 said had been confirmed by the</p> <p>22 GWAS studies.</p> <p>23 BY DR. THOMPSON:</p> <p>24 Q. Is it your testimony that</p>	<p>1 not what we're discussing. We're</p> <p>2 not discussing the produced</p> <p>3 documents from Dr. Saed.</p> <p>4 THE WITNESS: We can go</p> <p>5 through his CV, and I'm happy to</p> <p>6 point out which papers I read.</p> <p>7 DR. THOMPSON: Okay. Let's</p> <p>8 go ahead and do that.</p> <p>9 THE WITNESS: So Number 1.</p> <p>10 Number 2 is not relevant.</p> <p>11 Number 3 is not relevant.</p> <p>12 BY DR. THOMPSON:</p> <p>13 Q. But, you'll agree that those</p> <p>14 references are not included --</p> <p>15 A. I didn't read them. Like I</p> <p>16 said --</p> <p>17 Q. Let me finish my question.</p> <p>18 MS. SHARKO: Wait. She's</p> <p>19 going to ask a new question.</p> <p>20 BY DR. THOMPSON:</p> <p>21 Q. That -- you'll agree that</p> <p>22 those references were not included on</p> <p>23 either your reference list or your</p> <p>24 materials considered list, correct?</p>
Page 355	Page 357
<p>1 you read every article that was included</p> <p>2 in Dr. Saed's report?</p> <p>3 A. I definitely looked at every</p> <p>4 article that he authored that is in his</p> <p>5 report. I can't remember if I read every</p> <p>6 word. But I definitely looked at each of</p> <p>7 them to see if I thought they were</p> <p>8 directly relevant. And I probably read a</p> <p>9 large fraction of them.</p> <p>10 Q. And why are those not</p> <p>11 included on your reference list?</p> <p>12 A. Because I was referring to</p> <p>13 them from his report.</p> <p>14 MS. SHARKO: I mean, just so</p> <p>15 there's no confusion. We gave Dr.</p> <p>16 Neel all the exhibits and all the</p> <p>17 documents that Dr. Saed produced</p> <p>18 that's on Page 40. We didn't take</p> <p>19 the time to list all that out.</p> <p>20 MS. O'DELL: That's not what</p> <p>21 he was referring to in terms -- he</p> <p>22 wasn't referring to produced</p> <p>23 documents. I think he was</p> <p>24 referring to references. That's</p>	<p>1 A. Well, because for the</p> <p>2 standpoint of my report, the fact that</p> <p>3 it's not germane to the issue here is</p> <p>4 what I was saying.</p> <p>5 In other words, if you look</p> <p>6 on Page 17, he makes this statement that</p> <p>7 ovarian cancer patients manifest</p> <p>8 significantly decreased levels of</p> <p>9 antioxidants and higher level of</p> <p>10 oxidants.</p> <p>11 I say regardless of whether</p> <p>12 the statement is true, it's a non</p> <p>13 sequitur. That's why I didn't list it as</p> <p>14 a reference. And I didn't consider those</p> <p>15 papers as part of this report and part of</p> <p>16 my opinion about, you know, the role of</p> <p>17 talc and ovarian cancer because this is</p> <p>18 not relevant.</p> <p>19 So I looked at the paper.</p> <p>20 Q. You're saying that statement</p> <p>21 in A comes from one of his other papers?</p> <p>22 A. He references the other</p> <p>23 paper, but the issue is not relevant to</p> <p>24 this case, because it has to do with</p>

Page 358	Page 360
<p>1 what's happened in already developed 2 ovarian cancer. And the issue at hand is 3 whether talc produces oxidative stress 4 which causes ovarian cancer which occurs 5 before fully blown ovarian cancer. 6 So that's why I pointed out 7 it's not relevant. 8 Q. All right. So I'm entitled 9 to know every paper that you relied upon 10 for your opinions. 11 So if you need to go through 12 Dr. Saed's CV and you can tell me which 13 of these papers you read and relied upon, 14 let's go ahead and do that. 15 MS. SHARKO: I object to the 16 form of the question. There's a 17 difference between reading and 18 relied upon. Which do you want? 19 DR. THOMPSON: Okay. Well, 20 let's go with materials 21 considered, the title of his 22 reference list. 23 BY DR. THOMPSON: 24 Q. So --</p>	<p>1 DR. THOMPSON: That's -- 2 Dr. Neel -- 3 MS. SHARKO: I don't agree 4 with that. But anyway, go ahead. 5 BY DR. THOMPSON: 6 Q. Were all the -- were all the 7 publications that you reviewed of 8 Dr. Saed's included within the exhibits 9 from his deposition? 10 A. I'd have to look at his 11 deposition to be sure. 12 Q. Well, it was in your file, 13 right? 14 A. I know, but I don't have a 15 photographic memory of everything that 16 was in his deposition. 17 Q. And you didn't bring 18 anything with you here today? 19 A. I didn't bring anything with 20 me. 21 MS. SHARKO: Which is the 22 agreement of counsel. 23 MS. O'DELL: No, it's not. 24 We requested that materials that</p>
Page 359	Page 361
<p>1 DR. THOMPSON: And none of 2 Saed's papers were on the 3 materials considered list, either 4 in the original or the 5 supplemental. So -- 6 MS. SHARKO: So I disagree 7 with you on that because the 8 exhibits to the depositions are, 9 the depositions are, his report 10 is, and his reported whatever it 11 was attached to it. 12 So I take issue with that. 13 That being said, if you want 14 to -- if you want to have Dr. Neel 15 go through the CV, the part of the 16 CV that's marked as Exhibit 29, 17 and tell you which ones he's read, 18 sure, you can do that. 19 MS. O'DELL: Exhibits to -- 20 exhibits to Dr. Saed's deposition 21 did not cover his previous 22 publications. So to suggest 23 otherwise, I think would be 24 incorrect.</p>	<p>1 were considered be brought to the 2 deposition. 3 There was no agreement that 4 those would not be brought here 5 today. You've asserted 6 objections, and some of which we 7 take issue with. But there's no 8 agreement that the materials would 9 not be brought. 10 MR. TISI: And I must tell 11 you, we have brought -- we have 12 brought every -- boxes of material 13 to every one of the depositions. 14 So this is another example 15 of you representing something that 16 really didn't happen. 17 So if you would tell us 18 where we agreed to that, I haven't 19 seen it. Because we've got boxes 20 and boxes and we gave it to you, 21 for example. 22 MS. SHARKO: There was no -- 23 Mr. Tisi, I'm not going to waste 24 your side's time having an</p>

<p style="text-align: right;">Page 362</p> <p>1 argument.</p> <p>2 MR. TISI: Good, because you</p> <p>3 can't because there was no such</p> <p>4 agreement.</p> <p>5 You make these kinds of</p> <p>6 assertions repeatedly and they are</p> <p>7 just not true. So you --</p> <p>8 MS. SHARKO: You are totally</p> <p>9 wrong, Mr. Tisi.</p> <p>10 MR. TISI: So tell me where</p> <p>11 it is we agreed that he could not</p> <p>12 bring materials relied on, when we</p> <p>13 asked them in the notice of</p> <p>14 deposition.</p> <p>15 MS. SHARKO: We served</p> <p>16 objections to the deposition</p> <p>17 notice, which you have.</p> <p>18 MR. TISI: That's not an</p> <p>19 agreement.</p> <p>20 MS. SHARKO: There was no</p> <p>21 agreement to bring all the stuff</p> <p>22 that everybody reviewed. If</p> <p>23 there's something specific you</p> <p>24 want, let's figure it out and get</p>	<p style="text-align: right;">Page 364</p> <p>1 on.</p> <p>2 MR. TISI: Okay. Well, tell</p> <p>3 me where it is. Tell me where we</p> <p>4 agreed not to bring information</p> <p>5 relied on.</p> <p>6 MS. SHARKO: No.</p> <p>7 MR. TISI: Okay.</p> <p>8 MS. O'DELL: I think, tell</p> <p>9 us where and tell us who you</p> <p>10 believe made that agreement,</p> <p>11 because I can tell you the only</p> <p>12 other person that would have the</p> <p>13 authority to make that agreement</p> <p>14 is Michelle. She is not here. It</p> <p>15 would be Chris or myself.</p> <p>16 This is not true. So let's</p> <p>17 move on. But if you're going to</p> <p>18 take the position that you're not</p> <p>19 going to bring materials for</p> <p>20 experts in these depositions, then</p> <p>21 we need to take it up with Judge</p> <p>22 Pisano, because that's clearly not</p> <p>23 in compliance with the rules.</p> <p>24 MS. SHARKO: So -- so if</p>
<p style="text-align: right;">Page 363</p> <p>1 it.</p> <p>2 MR. TISI: But he's -- but</p> <p>3 you said there was an agreement of</p> <p>4 counsel not to bring things, which</p> <p>5 is totally different than you</p> <p>6 objecting to something on the</p> <p>7 notice of deposition.</p> <p>8 MS. SHARKO: I disagree with</p> <p>9 you, Mr. Tisi.</p> <p>10 MR. TISI: Okay. Well, I</p> <p>11 think the record will --</p> <p>12 MS. SHARKO: You constantly</p> <p>13 make misrepresentations, Mr. Tisi,</p> <p>14 but that's --</p> <p>15 MR. TISI: That's a</p> <p>16 deflection. That's a deflection.</p> <p>17 You made an assertion,</p> <p>18 Susan, that there was an agreement</p> <p>19 of counsel not to bring</p> <p>20 information to the deposition that</p> <p>21 the witness relied on. That's not</p> <p>22 true. So --</p> <p>23 MS. SHARKO: I disagree -- I</p> <p>24 disagree with you. But let's move</p>	<p style="text-align: right;">Page 365</p> <p>1 there's -- there are things that</p> <p>2 you think should be brought to the</p> <p>3 depositions, let's talk about that</p> <p>4 afterwards.</p> <p>5 MR. TISI: Everything that</p> <p>6 was in the notice of deposition.</p> <p>7 Every -- because I -- you know,</p> <p>8 we -- we have depositions coming</p> <p>9 up and unless there's some basis</p> <p>10 like privilege or something like</p> <p>11 that, we expect you to bring them</p> <p>12 to the deposition.</p> <p>13 MS. SHARKO: All right. I'm</p> <p>14 not going to have this</p> <p>15 discussion --</p> <p>16 MR. TISI: Of course you</p> <p>17 don't want to.</p> <p>18 MS. SHARKO: -- now on the</p> <p>19 record.</p> <p>20 MR. TISI: Of course you</p> <p>21 don't want to. Because -- because</p> <p>22 we did it. We did it and you</p> <p>23 didn't.</p> <p>24 MS. SHARKO: Mr. Tisi, let's</p>

<p style="text-align: right;">Page 366</p> <p>1 move on.</p> <p>2 I'm happy to --</p> <p>3 MR. TISI: Okay.</p> <p>4 MS. SHARKO: Leigh, I'm</p> <p>5 happy to talk to you afterwards or</p> <p>6 tomorrow. You'll probably be in</p> <p>7 Atlantic City, right?</p> <p>8 MS. O'DELL: We'll see.</p> <p>9 MS. SHARKO: We'll see?</p> <p>10 Okay.</p> <p>11 The judge changed the time,</p> <p>12 did you see that?</p> <p>13 MS. O'DELL: I did see that.</p> <p>14 BY DR. THOMPSON:</p> <p>15 Q. Okay.</p> <p>16 A. I looked through -- so I</p> <p>17 want to clarify what I meant.</p> <p>18 So I read several of these</p> <p>19 papers to see if they were relevant and</p> <p>20 I -- if I thought they were irrelevant, I</p> <p>21 said they were irrelevant.</p> <p>22 But if you want to know</p> <p>23 which ones, it's what he cited in his</p> <p>24 paper. But I -- I mean --</p>	<p style="text-align: right;">Page 368</p> <p>1 A. Yes, but several -- several</p> <p>2 of them have, you know, statements which</p> <p>3 are not true, like the thing about the</p> <p>4 SNPs.</p> <p>5 Q. Was the methodology that was</p> <p>6 used in the previous publications and</p> <p>7 peer reviewed relevant at all?</p> <p>8 MS. SHARKO: Object to the</p> <p>9 form of the question.</p> <p>10 THE WITNESS: Yeah, I don't</p> <p>11 know which particular methodology</p> <p>12 or paper you're referring to.</p> <p>13 BY DR. THOMPSON:</p> <p>14 Q. Well, I'm saying if Dr. Saed</p> <p>15 used the same or similar methods</p> <p>16 publishing this paper that he did in</p> <p>17 previous papers, is that relevant?</p> <p>18 A. He didn't use the same</p> <p>19 method. The -- the earlier work was just</p> <p>20 based on small SNP analysis. This was</p> <p>21 based on use of panels of SNPs, arrays of</p> <p>22 SNPs. It's a -- it's a new -- relatively</p> <p>23 -- it's a more modern method that's</p> <p>24 available in the earlier papers.</p>
<p style="text-align: right;">Page 367</p> <p>1 Q. Okay. Let's --</p> <p>2 A. -- there are very few</p> <p>3 additional papers that are even cited by</p> <p>4 him in his paper, in his report, that are</p> <p>5 relevant.</p> <p>6 Q. Okay. First off, let me</p> <p>7 just ask you, are any of the papers</p> <p>8 listed on Dr. Saed's CV relevant in your</p> <p>9 mind?</p> <p>10 A. The most relevant one is</p> <p>11 the -- is the current one, which is the</p> <p>12 one that was in press. And that's the</p> <p>13 one that I criticized the most</p> <p>14 specifically.</p> <p>15 Many of the other ones are</p> <p>16 cited by Dr. Saed as relevant, but they</p> <p>17 aren't relevant in my opinion, as I state</p> <p>18 in my report.</p> <p>19 So, for example --</p> <p>20 Q. So -- okay. So no -- none</p> <p>21 of Dr. Saed's previous publications that</p> <p>22 are relevant in your opinion with the</p> <p>23 exception of the one just published; is</p> <p>24 that correct?</p>	<p style="text-align: right;">Page 369</p> <p>1 Q. But you'll agree with me</p> <p>2 that there -- there's a lot of data in</p> <p>3 Dr. Saed's paper that goes beyond just</p> <p>4 the SNP analysis, correct?</p> <p>5 A. The SNP analysis is the only</p> <p>6 analysis which addresses the</p> <p>7 extraordinary claim of a genotype switch</p> <p>8 in response to talc treatment of cells.</p> <p>9 So that is the only data.</p> <p>10 What he should have done was</p> <p>11 carry out Sanger sequencing, since he's</p> <p>12 claiming that there is a wholesale change</p> <p>13 in a genetic content of a specific</p> <p>14 polynucleotide -- of a specific SNP</p> <p>15 within 72 hours of talc treatment which</p> <p>16 would be utterly unprecedented as far as</p> <p>17 I know in molecular biology.</p> <p>18 Q. Okay. Let's -- let's go</p> <p>19 ahead and have you identify what articles</p> <p>20 from Dr. Saed's CV that you considered.</p> <p>21 A. Oh. For example, on Page 30</p> <p>22 he said -- he had a paper, "Specific</p> <p>23 point mutations and key redox enzymes are</p> <p>24 associated with chemoresistance and</p>

Page 370	Page 372
<p>1 epithelial ovarian cancer." I looked at 2 that paper and immediately concluded that 3 it was not relevant to this litigation or 4 the question of my report because it has 5 to do with fully blown ovarian cancer. 6 So I looked at the paper, 7 but it's not relevant for this, so I 8 didn't cite it in my reference. 9 Q. So which -- 10 A. Similarly -- 11 Q. -- which paper was that? 12 A. Reference 9. 13 Q. Give me a number -- 14 A. Page 30. 15 Q. Okay. So that one you 16 looked at and determined it was not 17 relevant? 18 A. Correct. 19 Q. Let's just go through, 20 and -- 21 A. Similarly -- 22 Q. -- tell me if there are 23 others -- 24 A. Reference 15 addresses a</p>	<p>1 how to answer that, because 2 there's obviously a legal issue 3 here that I don't understand. 4 But, I mean, if I read 5 something and it's not relevant to 6 my opinions, does that mean that I 7 considered it? Okay. Well, in 8 that case... 9 MS. SHARKO: That wouldn't 10 be my interpretation, but if 11 that's your question. That's 12 fine. 13 BY DR. THOMPSON: 14 Q. Well, it's fine to go ahead 15 and tell us whether or not you -- go 16 ahead and circle the ones that you read 17 and I may ask you questions. 18 A. Sure. Reference 26, I read. 19 It was relevant to something I'm 20 interested in, but it wasn't at all 21 germane. So I don't know how you would 22 count that one. 23 MS. SHARKO: By the way we 24 have the references in the</p>
Page 371	Page 373
<p>1 similar subject. Not relevant. 2 Q. Oh, okay. 3 A. Reference -- I'm just 4 referring to -- 5 Q. Do you have the exhibit 6 there? 7 A. Yes. 8 Q. Would you go ahead and mark 9 on the exhibit? 10 A. I thought I'm not allowed to 11 mark the exhibits. 12 Q. You are if we ask you to. 13 A. Okay. Sure. 14 Q. Go ahead and -- just so 15 we'll have the record. Go ahead and mark 16 which ones that you considered. 17 MS. SHARKO: Considered 18 meaning read? 19 DR. THOMPSON: I'm just 20 using the language that's in the 21 statute, materials considered, and 22 what's on his reliance list -- on 23 his materials considered list. 24 THE WITNESS: I don't know</p>	<p>1 doctor's report in the other room 2 if you want them if you can't find 3 a paper. 4 DR. THOMPSON: Okay. 5 Thanks. 6 THE WITNESS: Again, 45 7 would fall under the same 8 category. That's it. Oh, wait 9 the review articles. 10 BY DR. THOMPSON: 11 Q. Dr. Neel, if you're 12 finished. 13 A. No, I didn't look at the 14 reviews. You can have your pen back too. 15 I am a pen stealer. I admit to that. 16 Q. So Dr. Neel, let me just ask 17 you about the articles that are circled 18 on Dr. Saed's CV, Exhibit 29, and have 19 you tell me whether these were papers 20 that you relied upon for your opinions or 21 decided were not relevant or any comments 22 that you want to make. 23 A. Sure. 24 MS. SHARKO: Except now he</p>

<p style="text-align: right;">Page 374</p> <p>1 doesn't have a copy of it in front 2 of him. 3 DR. THOMPSON: That's true. 4 THE WITNESS: You can keep 5 handing it back and forth to me. 6 DR. THOMPSON: No, let me -- 7 or maybe share Ms. Sharko's copy. 8 MS. SHARKO: Okay. So my 9 copy won't have circles on it. 10 DR. THOMPSON: Right. I'll 11 tell you a number and you can tell 12 me. 13 That's probably even better. 14 BY DR. THOMPSON: 15 Q. On that exhibit, let's go 16 through the ones that are circled. If 17 you could just mark relevant or 18 irrelevant. "I" for irrelevant -- "I" 19 for irrelevant and "R" for relevant. How 20 is that? 21 MS. SHARKO: Those are the 22 only two choices? 23 BY DR. THOMPSON: 24 Q. If you have a different</p>	<p style="text-align: right;">Page 376</p> <p>1 my opinion that, you know, he's 2 misinterpreting the data. So I don't 3 know how to -- how to write that. 4 Q. And that paper was published 5 in Gynecologic Oncology, right? 6 A. Yes. 7 Q. And peer-reviewed, right? 8 A. Yes, as I said before, the 9 very fact that -- if it's not 10 peer-reviewed, it's completely unreliable 11 until it's peer-reviewed. But the fact 12 that it's been peer-reviewed doesn't make 13 it right. 14 Q. Do you know the -- 15 MS. SHARKO: Well, wait. 16 He's still going through the -- 17 through the last task. 18 THE WITNESS: I think 19 that's -- that's -- I think that's 20 all of them. Yeah. Okay. I 21 marked them all. 22 BY DR. THOMPSON: 23 Q. Okay. Thank you. Do you 24 recognize any of the other authors on</p>
<p style="text-align: right;">Page 375</p> <p>1 choice, we can have a write-in candidate. 2 A. How about not directly 3 relevant, although it was cited by him as 4 relevant. 5 Ditto, not directly 6 relevant, although he asserted it was. 7 As I said, as I recall the 8 only one that's directly relevant is the 9 more recent one. And all the other ones 10 are claimed as being relevant but they're 11 off point, in my opinion. I'm going to 12 write the same thing on all the other 13 ones. There aren't that many, because 14 most of these papers are not directly 15 relevant. 16 So for example, Reference 52 17 is not -- this is the one where he, I 18 believe, shows -- I don't have the paper 19 in front of me. We'd have to look at it. 20 But I believe that's the paper where he 21 claims that myeloperoxidase expressed in 22 ovarian cancer cells. 23 So that's not relevant to 24 the topic at hand, but it is relevant to</p>	<p style="text-align: right;">Page 377</p> <p>1 these paper as you look through it? By 2 memory, name the authors that you 3 recognize. 4 A. I don't remember -- I mean, 5 I don't -- 6 Q. Could you just glance 7 through and see if you -- 8 A. Sure. 9 Q. -- recognize any of the 10 other authors. 11 A. Sure. 12 MS. SHARKO: On the ones 13 that he marked, right? 14 THE WITNESS: I recognize 15 Fletcher, because I know that 16 she's in the lab. I recognize her 17 name from the deposition. But I 18 don't know any of the other 19 authors. Fletcher again. 20 BY DR. THOMPSON: 21 Q. So is it fair to say, 22 Dr. Neel, that you don't know the 23 reputations of any of Dr. Saed's 24 co-authors on these papers?</p>

<p style="text-align: right;">Page 378</p> <p>1 A. So far, that's fair to say, 2 yes. But I believe that the overwhelming 3 majority of them are people who are 4 working in his lab. 5 Q. Do you know that or are you 6 guessing? 7 A. No, I know that from the 8 papers that I remember reading, I think 9 most of them, it was from one lab. But I 10 could be -- we can go through each 11 individual paper if you want. But that 12 reputation -- reputation is not relevant 13 to me. 14 What's relevant to me is my 15 reading of the papers and assessment of 16 their scientific quality. And that's 17 what I did, and that's the basis for my 18 conclusions on Page 23, Point K. 19 Q. Let's switch gears a little 20 bit, Dr. Neel. 21 You looked at other papers 22 directly related to molecular effects of 23 talc or talcum powder as well, correct? 24 A. Most of which, we've already</p>	<p style="text-align: right;">Page 380</p> <p>1 Q. And you had actually quite a 2 few criticisms of this paper as well? 3 A. Yes. 4 Q. Correct? 5 A. Yes. Starting with the fact 6 that it's published in a journal that's 7 not really relevant to ovarian cancer or 8 cancer, Phytotherapy Research. I don't 9 think I've ever seen a paper on ovarian 10 cancer in Phytotherapy Research. 11 Q. But you'll agree that the 12 paper at least deals with ovarian cells 13 cultures and molecular effects, right? 14 A. A small part of the paper, 15 yeah. Yes. 16 Q. This paper was 17 peer-reviewed, right? 18 A. By somebody who reviews for 19 Phytotherapy Research, which is highly 20 unlikely to be anyone who is a credible 21 ovarian cancer researcher. 22 Q. And in the abstract of this 23 paper, the authors state, "Talc increased 24 proliferation, induced neoplastic</p>
<p style="text-align: right;">Page 379</p> <p>1 discussed. But yes, everything that's in 2 my report is what I looked at. 3 Q. Let's talk about that 4 Buz'Zard paper that you read and included 5 in your report on Page 25. 6 A. Yes. Buz'Zard and Lau. 7 Q. I could have swore I put 8 those stickers right where I could find. 9 There they are. 10 DR. THOMPSON: This will be 11 Exhibit 30, the paper by Buz'Zard. 12 (Document marked for 13 identification as Exhibit 14 Neel-30.) 15 MS. SHARKO: Do we have a 16 29? 17 THE WITNESS: Maybe that was 18 the CV. 19 MS. SHARKO: Oh yeah. CV 20 was 29. I'm sorry. 21 BY DR. THOMPSON: 22 Q. Do you recall reading this 23 paper? 24 A. Absolutely.</p>	<p style="text-align: right;">Page 381</p> <p>1 transformation, and increased ROS 2 generation time dependently in the 3 ovarian cells and dose dependently in the 4 PNM." 5 Did I read that correctly? 6 A. Yes, you read the statement 7 correctly. 8 Q. And is it your opinion that 9 those statements do not actually reflect 10 what the experiments demonstrated? 11 A. Yes. It's my -- it's my 12 contention that this paper is highly 13 flawed in multiple ways, starting with -- 14 do you want me to tell you all the ways 15 that it's flawed? 16 Q. Sure. 17 A. Starting with the fact that 18 we have no idea what a -- if there -- if 19 talc does get from the perineum into the 20 fallopian tube or the ovarian surface 21 epithelial region, we have no idea of 22 what a relevant dose is. So picking 23 these doses has no biological relevance. 24 In fact, I don't think you</p>

<p style="text-align: right;">Page 382</p> <p>1 can actually study the question unless 2 you have an idea of the dose of the agent 3 that gets to the relevant tissue. So the 4 first problem is the design of the 5 experiments is intrinsically flawed. 6 The second point -- 7 Q. Can we go one at a time -- 8 A. Sure. 9 Q. -- just because I have 10 question -- 11 A. Sure. Yeah, you asked me 12 to -- 13 Q. It will be easier -- yeah. 14 A. So that's my first problem. 15 Q. Aren't in vitro studies 16 frequently done for mechanistic purposes 17 and not necessarily to determine a 18 relevant dose? 19 A. It's well known that the 20 only relevant studies that are done in 21 vitro are done with a relevant dose of 22 the agent that you're testing. 23 So I can only comment on 24 well-designed and well-performed</p>	<p style="text-align: right;">Page 384</p> <p>1 powder that would be relevant? 2 A. I think it would be 3 impossible to do a compelling study until 4 you first answered the question of 5 whether perineum -- talc applied to the 6 perineum of a woman gets to the ovary and 7 at what dose -- 8 Q. How do you -- 9 A. The fallopian tube. 10 Q. How do you ascertain that 11 information? 12 A. It's not my -- I would have 13 to sit down and think it through. That's 14 not my purpose here today. 15 My purpose is not to do the 16 experiments for them. My purpose is to 17 evaluate the published data. 18 And my opinion is that the 19 study starts out being flawed by not 20 knowing anything about a relevant dose. 21 It's their obligation to figure out a 22 relevant dose, not mine. It's my 23 obligation to read their paper and decide 24 whether it's scientifically credible.</p>
<p style="text-align: right;">Page 383</p> <p>1 experiments, not poorly designed and 2 poorly performed experiments. 3 Q. How would you know a 4 relevant dose if you wanted to look at 5 talcum powder in vitro and how it would 6 relate to women who are using talcum 7 powder regularly on their perineum? 8 A. That's exactly the point. 9 Q. So are the -- would all 10 molecular studies be worthless? 11 A. Until you can define a 12 reasonable dose, it doesn't -- you can't 13 do an experiment that's relevant to the 14 question at hand. 15 If you just go dumping talc 16 at various levels onto cells, it may have 17 absolutely no -- it probably has 18 absolutely no relevance to what happens 19 when you apply talc to the perineum of a 20 woman, and if and whether any degree of 21 talc gets to -- to the relevant tissue. 22 Q. So in your opinion, with our 23 current knowledge, it would be impossible 24 to do a molecular study with talcum</p>	<p style="text-align: right;">Page 385</p> <p>1 But that's the -- that's only the first 2 of many weaknesses of this study. 3 Q. We'll get -- we'll get to 4 some -- let me finish my question here 5 and then we'll get to the others. 6 Assuming that you did not 7 have a conflict of interest policy at 8 your institution, could you design a 9 study, a molecular study that you think 10 could be relevant to studying the issue 11 that we are talking about today? 12 A. I don't know. I haven't 13 really given it any thought. I haven't 14 given it significant thought. Maybe. 15 I'd have to think about it for a while. 16 Q. Okay. Let's go on with 17 your -- your criticisms. 18 Are these the same that are 19 outlined in your report? 20 A. Yes. 21 Q. Or are there additional 22 ones? 23 A. Yes, those are exactly the 24 criticisms. But I'm happy to go through</p>

<p style="text-align: right;">Page 386</p> <p>1 each of them if you want.</p> <p>2 Q. Let's go ahead and go</p> <p>3 through them.</p> <p>4 A. Okay. Well, granular --</p> <p>5 most of the study, a large fraction of</p> <p>6 the study concerns granulosis cells which</p> <p>7 are not relevant to epithelial ovarian</p> <p>8 cancer of any type.</p> <p>9 Q. So is it your opinion that</p> <p>10 seeing biological effects on cells from</p> <p>11 anything other than tubal epithelium are</p> <p>12 irrelevant?</p> <p>13 A. Well, even if they had, you</p> <p>14 know, primary ovarian surface epithelium,</p> <p>15 that might be relevant because I think</p> <p>16 there is some evidence that some ovarian</p> <p>17 cancer come from the OSE, ovarian surface</p> <p>18 epithelial, OSE.</p> <p>19 But these cells are already</p> <p>20 transformed with SV40 large T antigen.</p> <p>21 And SV40 large T antigen inactivates the</p> <p>22 two major oncogenic pathways. It</p> <p>23 activates all members of the RV family</p> <p>24 and it inactivates p53. So these cells</p>	<p style="text-align: right;">Page 388</p> <p>1 It's well known that soft</p> <p>2 agar transformation in human cells is not</p> <p>3 predictive of -- of tumorigenicity which</p> <p>4 is the issue at hand.</p> <p>5 And the -- if you look</p> <p>6 carefully at the data, the -- the</p> <p>7 purported pro-oncogenic effects on</p> <p>8 cellular proliferation and on ROS occur</p> <p>9 at two different doses of talc.</p> <p>10 So notwithstanding my</p> <p>11 criticism about the dose in the first</p> <p>12 place, it's not known which of these</p> <p>13 doses would be relevant.</p> <p>14 So I think that pretty much</p> <p>15 covers it.</p> <p>16 Oh yeah, the</p> <p>17 polymorphonuclear leukocyte experiments</p> <p>18 are not relevant because, as we discussed</p> <p>19 earlier today, there is no evidence for</p> <p>20 white -- for poly -- or PMN infiltration</p> <p>21 into the premalignant lesions of -- of</p> <p>22 human fallopian lesions like STICs or</p> <p>23 stills or p53 signatures.</p> <p>24 So I don't really think</p>
<p style="text-align: right;">Page 387</p> <p>1 are already transformed.</p> <p>2 So if you're trying to</p> <p>3 investigate the effects of a potential</p> <p>4 initiating event, then this study is</p> <p>5 irrelevant.</p> <p>6 Plus it's well known that</p> <p>7 SV40 large T transformed cells are</p> <p>8 genetically unstable and any -- and</p> <p>9 different lines are different. So it's</p> <p>10 really not generally accepted that you</p> <p>11 use a study where you transform cells</p> <p>12 with SV40 large T and -- and use that to</p> <p>13 infer something about normal biology.</p> <p>14 So I think that's a serious</p> <p>15 weakness of this study.</p> <p>16 Q. Okay. Next?</p> <p>17 A. The third point is that they</p> <p>18 don't show any tumor genicity studies.</p> <p>19 It would have been very easy for them to</p> <p>20 take these cells, treat them with talc</p> <p>21 and then inject them into</p> <p>22 immunoincompetent mice and at least see</p> <p>23 if there's any evidence of</p> <p>24 transformation.</p>	<p style="text-align: right;">Page 389</p> <p>1 there's much in this paper to support the</p> <p>2 case that talc is pro-oncogenic.</p> <p>3 Q. And --</p> <p>4 A. It's a very poor quality</p> <p>5 journal and it's -- I don't think these</p> <p>6 authors have ever published on this again</p> <p>7 as far as I can tell.</p> <p>8 Q. Is it -- is it fair to say</p> <p>9 your criticisms of the Buz'Zard paper are</p> <p>10 similar to those of Dr. Saed's paper?</p> <p>11 A. No. They're -- they are</p> <p>12 different.</p> <p>13 Q. In terms of being flawed?</p> <p>14 A. Well, I mean I would say</p> <p>15 that it's like Anna Karenina. They are</p> <p>16 flawed in different ways.</p> <p>17 Q. Fair enough. Let's --</p> <p>18 and -- and the -- the results and</p> <p>19 mechanism that the authors are proposing</p> <p>20 in this paper are -- are not even</p> <p>21 plausible in your mind?</p> <p>22 A. Plausibility requires good</p> <p>23 experiments. These are bad experiments.</p> <p>24 So based on this set of data, there is</p>

<p style="text-align: right;">Page 390</p> <p>1 nothing that can be educed from this work 2 as to biological plausibility in my 3 opinion. 4 Q. Let's -- let's go next to 5 the Shukla paper. Do you remember -- 6 A. Shukla? 7 Q. -- seeing that paper? 8 A. I remember the paper -- I 9 remember the name. It's an unusual name 10 so I remember. But I don't recall the -- 11 I'd have to see the paper to actually 12 comment on it. 13 Q. I'll hand that to you now. 14 (Document marked for 15 identification as Exhibit 16 Neel-31.) 17 BY DR. THOMPSON: 18 Q. Did you review this paper, 19 Dr. Neel? 20 A. Yes. 21 Q. And I believe you discussed 22 this paper in your report as well, 23 correct? 24 A. I do. Can you tell me the</p>	<p style="text-align: right;">Page 392</p> <p>1 in the report. But let me just look at 2 it again. Oh, yeah. So again, this is 3 an SV40 Tag-immortalized 4 anchorage-dependent human ovarian 5 epithelial line, so it's -- 6 MS. SHARKO: You've got to 7 go much slower. Sorry. 8 THE WITNESS: Oh, I'm sorry. 9 On Page -- on Page 115 in the 10 left-hand column, midway through 11 under the methods, which I write 12 extensively, it's an -- the 13 authors use for ovarian surface 14 epithelial cells an SV40 15 Tag-immortalized, 16 anchorage-dependent human ovarian 17 epithelial cell line. 18 So this suffers from the 19 same issues that I just mentioned 20 for the Buz'Zard paper in that 21 it's using a cell line that 22 already has -- should I continue? 23 BY DR. THOMPSON: 24 Q. Yes, I'm sorry.</p>
<p style="text-align: right;">Page 391</p> <p>1 page though? 2 Q. Yes. 3 A. So I can make sure. 4 Q. It's Page 21. Beginning on 5 Page 21. 6 In this paper, the authors 7 reported -- 8 A. Hold on. I don't see it on 9 21. Can you tell me where it is on 21? 10 Q. Page 21 of your paper in the 11 last paragraph. 12 A. Oh, sure, yeah, yeah. 13 Sorry. It's in the middle. 14 Q. And in this paper the 15 authors report all -- alterations in gene 16 expression following exposure to asbestos 17 as well as talc in mesothelial and 18 ovarian surface cells, correct? 19 A. Yes. 20 Q. Do you have criticisms of 21 this paper? 22 A. Hold on. Let me go through 23 it again. It's been a while since I saw 24 it. And the criticisms that I have are</p>	<p style="text-align: right;">Page 393</p> <p>1 MS. SHARKO: Okay. 2 THE WITNESS: This paper 3 uses an SV40 Tag-immortalized 4 anchorage-dependent human ovarian 5 epithelial cell line which, 6 therefore, suffers from the same 7 issues that I raised earlier with 8 the paper by Buz'Zard and Lau in 9 that this -- these cell lines 10 are -- already suffered -- already 11 have had introduced a minimum of 12 two of the transforming events 13 that occur in ovarian cancer. 14 So the cell line is not 15 necessarily germane to the 16 initiating events of ovarian 17 cancer. That's the first thing. 18 The second thing is that the 19 paper primarily concerns, you 20 know, asbestos effects on 21 mesothelial cells, not so much the 22 effects of talc on ovarian 23 epithelial cells. 24 And if you look at the</p>

<p style="text-align: right;">Page 394</p> <p>1 changes. In fact, if you go to 2 Page 2009. In contrast to 3 LP9/TERT and NYU474 mesothelial 4 cells, that's referring to the 5 pleural mesothelial cells. 6 IOSE cells showed no 7 significant gene upregulation or 8 downregulation in response to 9 lower concentrations of asbestos 10 and no significant mRNA changes 11 were observed with non-fibrous 12 talc, fine titanium dioxide, or 13 glass beads at either time point. 14 So the relevant cell type 15 shows no changes in gene 16 expression, and the irrelevant 17 cell type shows minimal changes in 18 gene expression in response to 19 talc. 20 So again, I don't really 21 think that Dr. Saed's quote is 22 relevant. So if you read my 23 report on Page 21, I refer to 24 Shukla, et al., in the context of</p>	<p style="text-align: right;">Page 396</p> <p>1 these cells -- 2 Q. Well, my question is -- 3 A. -- in terms of gene 4 expression. 5 Q. -- as to the relevance. 6 A. Well, it's not -- it's not 7 relevant, and it's not -- it doesn't 8 support the claim that ovarian cancer is 9 caused by talc. So in that way it's not 10 relevant. 11 Q. Would you consider this 12 paper reliable? 13 A. Reliable? I mean, they 14 measured -- insofar -- so it's reliable 15 in the sense that they've used 16 established techniques, and I'm sure that 17 the gene expression data is correct. 18 Reliable insofar as one can draw 19 conclusions about asbestos or talc, I 20 have no comment about what a relevant 21 dose would be of asbestos, because I 22 haven't researched that issue. But I do 23 have a comment, the same comment that I 24 raised earlier about a difficulty in</p>
<p style="text-align: right;">Page 395</p> <p>1 Dr. Saed's citation, not -- not 2 because I think this is 3 necessarily germane. 4 I am responding to 5 Dr. Saed's claim it's germane and 6 showing that it isn't germane in 7 my opinion. 8 BY DR. THOMPSON: 9 Q. So your opinion -- 10 MS. SHARKO: He was reading 11 from 118, not 2009. 12 THE WITNESS: Oh, did I -- 13 DR. THOMPSON: I found it. 14 MS. SHARKO: You did. 15 THE WITNESS: I'm sorry. 16 MS. SHARKO: No problem. 17 THE WITNESS: Sorry. Thank 18 you. 19 BY DR. THOMPSON: 20 Q. And so this paper, in your 21 opinion, is not relevant for the issue 22 that we're discussing today? 23 A. Well, if anything, it says 24 there is almost no effect of talc on</p>	<p style="text-align: right;">Page 397</p> <p>1 knowing what would be a relevant dose of 2 talc. 3 But in this case, the doses 4 they chose had no significant effects. 5 So it's not germane unless the -- unless 6 the point is to say that talc doesn't 7 induce gene expression changes in the 8 human ovarian cells. 9 Q. If -- and is it your 10 understanding that this paper or these 11 authors used non fibrous talc in the 12 studies? 13 A. I don't recall. I have to 14 look at what they used. 15 Q. It's in the abstract or the 16 methods. 17 A. Well, I would prefer to use 18 the methods. 19 Q. Sure. 20 A. I have to look at it. I 21 have to go to the results because they 22 characterize the fibers. I'm not really 23 an expert in fibers. But I believe 24 Dr. Mossman is an expert for the</p>

<p style="text-align: right;">Page 398</p> <p>1 defendant. So I think that she would 2 probably be better at explaining this 3 than I. 4 Yes, they claim that it's 5 non-fibrous talc. But again, I'm not an 6 expert in mineralogy or geology. So I 7 can't comment on the quality of their 8 evaluation. But I will say that it's 9 non-fibrous talc, according to the paper. 10 Q. And if Baby Powder were 11 shown to contain fibrous talc or 12 asbestos, how would that change your 13 opinions regarding the paper? 14 A. Well, it would just make 15 this paper even more irrelevant because 16 they didn't use Johnson & Johnson's 17 products. 18 Q. Do you know Dr. Mossman? 19 A. I don't know her. I know of 20 her reputation, but I don't know her. 21 Q. And you haven't spoken to 22 her -- 23 A. No. 24 Q. -- regarding this case?</p>	<p style="text-align: right;">Page 400</p> <p>1 familiar, Dr. Neel? 2 A. Yes. 3 Q. And did you read this paper? 4 A. A while ago, yes. 5 Q. Do you -- 6 A. I don't remember if I 7 actually -- was there a place in my 8 report that you want to discuss here? 9 Q. I don't believe that -- oh, 10 actually, I think you did discuss this in 11 here. Let me find it. Yes, it's on Page 12 24. 13 A. 24. I thought I remember 14 typing that. Yes. 15 Q. And do you have criticisms 16 regarding this paper? 17 A. Yes. As outlined in my 18 report on Page 24. 19 Q. And what are those? 20 A. These authors measured the 21 effects of talc on A549 cells, which are 22 lung cancer cells, and found ROS 23 production, oxidation of cellular lipids, 24 and DNA damage.</p>
<p style="text-align: right;">Page 399</p> <p>1 A. I've never met her or spoken 2 to her. 3 Q. I believe you had two papers 4 by Dr. Akhtar on your materials 5 considered list. Does that sound 6 familiar? 7 A. Yeah. I don't know if 8 that's the -- I didn't know how to 9 pronounce that name. 10 Q. I don't either so you're -- 11 does anyone? 12 A. It sounds like it's right. 13 A-H-K or something? 14 MS. SHARKO: That's 15 Exhibit 32. 16 (Document marked for 17 identification as Exhibit 18 Neel-32.) 19 DR. THOMPSON: 32 is the 20 Akhtar paper. 21 BY DR. THOMPSON: 22 Q. "The Primary Role of Iron 23 Mediated Lipid Peroxidation." 24 Does this paper look</p>	<p style="text-align: right;">Page 401</p> <p>1 So, again, these are already 2 established lung cancer cells. So I 3 don't see the relevance to the question 4 of initiation of ovarian cancer. That's 5 first thing. 6 The second thing is that -- 7 the same issues having to do with dose 8 are germane here. And I guess I should 9 see -- I don't remember which form of 10 talc they used. Yeah, so commercial 11 talc. So again, those are my main 12 criticisms. 13 They use dose -- again, as I 14 said, it's not clear as the dosage used 15 here or seen here relate to the small 16 number of particles that are presumably 17 found in the reproductive tract, if 18 they're there at all. 19 Q. Are you aware that Dr. Saed 20 used the same dosage as Dr. Akhtar 21 reported in his paper? 22 A. I'd have to look to be sure. 23 But perhaps. Dr. Saed's papers are 24 seriously flawed, as we've already</p>

<p style="text-align: right;">Page 402</p> <p>1 discussed.</p> <p>2 Q. Yeah, I understand your</p> <p>3 opinion as to that. The author's first</p> <p>4 sentence in the abstract is, "Talc</p> <p>5 particles, the basic ingredient in</p> <p>6 different kinds of talc-based cosmetic</p> <p>7 and pharmaceutical products, pose a</p> <p>8 health risk to pulmonary and ovarian</p> <p>9 systems due to domestic and occupational</p> <p>10 exposures."</p> <p>11 Do you disagree with that</p> <p>12 statement --</p> <p>13 A. Yes.</p> <p>14 Q. -- that Dr. Akhtar makes?</p> <p>15 A. Yes.</p> <p>16 Q. Do you think that Akhtar</p> <p>17 is -- Dr. Akhtar is not credible?</p> <p>18 A. I have no knowledge as to</p> <p>19 Dr. Akhtar. I have never met him. Don't</p> <p>20 know anything about him. Don't know his</p> <p>21 reputation and can't comment on it.</p> <p>22 Q. This paper was peer reviewed</p> <p>23 and published?</p> <p>24 A. Yes. And I also can't</p>	<p style="text-align: right;">Page 404</p> <p>1 glutathione depletion."</p> <p>2 Those were at least some of</p> <p>3 the same things that Dr. Saed studied,</p> <p>4 correct?</p> <p>5 A. No, actually -- no, that's</p> <p>6 not correct. Actually, the major</p> <p>7 weakness of Dr. Saed's paper is he did</p> <p>8 not measure. As I said earlier, if you</p> <p>9 are going to claim a difference in redox</p> <p>10 balance, you have to measure redox</p> <p>11 balance by measuring ROS generation in</p> <p>12 the form DCF fluorescence or other types</p> <p>13 of ROS sensor assays. Lipid peroxidation</p> <p>14 by BODIPY staining or other methods like</p> <p>15 -- oxidative damage to DNA by ADG</p> <p>16 staining, none of which Dr. Saed did, as</p> <p>17 I said earlier.</p> <p>18 Q. Did you -- do you have any</p> <p>19 other criticisms of this paper?</p> <p>20 A. My -- my major point about</p> <p>21 this paper as I've said already, is that</p> <p>22 it concerns already developed lung cancer</p> <p>23 cells and it is well known in the</p> <p>24 scientific literature that there is</p>
<p style="text-align: right;">Page 403</p> <p>1 comment, since I'm not a toxicologist, on</p> <p>2 the quality of this journal. But I think</p> <p>3 it's probably not a high impact journal</p> <p>4 or a high quality journal.</p> <p>5 Q. Do you know if nanoparticles</p> <p>6 would apply to Johnson's Baby Powder?</p> <p>7 A. As I said, I am not -- not a</p> <p>8 mineralogist, I'm not a toxicologist. I</p> <p>9 can't comment on any of that.</p> <p>10 Q. So you --</p> <p>11 A. I don't have any</p> <p>12 professional opinion on that.</p> <p>13 Q. So you really have no idea</p> <p>14 as to the particle size of Johnson's Baby</p> <p>15 Powder?</p> <p>16 A. I have no idea as to the</p> <p>17 particle size.</p> <p>18 Q. And the authors a little</p> <p>19 further down in the abstract state, "Both</p> <p>20 varieties of talc nanoparticles</p> <p>21 differentially induce lipid peroxidation</p> <p>22 which was correlated with the pattern of</p> <p>23 lactate dehydrogenase leakage, reactive</p> <p>24 oxygen species generation, and</p>	<p style="text-align: right;">Page 405</p> <p>1 differences between the effects of ROS in</p> <p>2 cancer cells that are already</p> <p>3 established, and in particular, in cancer</p> <p>4 cell lines that have been passive for</p> <p>5 many years, and in particular, in</p> <p>6 different types of cancer cells than are</p> <p>7 present in normal cells.</p> <p>8 So the paper is -- is not</p> <p>9 germane in my opinion to the question of</p> <p>10 whether talc causes ROS changes and</p> <p>11 reactive oxygen induced damage in primary</p> <p>12 fallopian tube epithelium or primary</p> <p>13 ovarian surface epithelium.</p> <p>14 That is the relevant</p> <p>15 question. Notwithstanding all the issues</p> <p>16 about dose that we've talked about.</p> <p>17 Q. You'll agree though that the</p> <p>18 authors of this paper at least thought</p> <p>19 that their experiment was relevant for</p> <p>20 ovarian cancer, right?</p> <p>21 A. I have no idea --</p> <p>22 MR. LOCKE: Objection.</p> <p>23 BY DR. THOMPSON:</p> <p>24 Q. Well, they stated it that,</p>

<p style="text-align: right;">Page 406</p> <p>1 in the first sentence, that --</p> <p>2 A. They -- they said that --</p> <p>3 Q. -- it poses a risk to</p> <p>4 pulmonary and ovarian systems.</p> <p>5 A. Well, that's their opinion.</p> <p>6 That doesn't say whether they thought</p> <p>7 they were -- whether they thought it was</p> <p>8 relevant. All they can say is that it --</p> <p>9 that assuming that everything in this</p> <p>10 paper is correct, in terms of the</p> <p>11 measurements and all that, which I have</p> <p>12 no reason to question, they can't say</p> <p>13 anything about dose, and they can't say</p> <p>14 anything about the relevant cells.</p> <p>15 So, cells are not cells.</p> <p>16 It's not like, you know, parts is parts</p> <p>17 in Perdue chicken.</p> <p>18 Q. What's you -- what's your</p> <p>19 basis for opinion that the -- the cells</p> <p>20 used in this experiment are not relevant</p> <p>21 for ovarian surface epithelium?</p> <p>22 A. Well, as I've already said,</p> <p>23 they are lung cancer cells. They -- they</p> <p>24 are a mutation. So A-549 cells have KRAS</p>	<p style="text-align: right;">Page 408</p> <p>1 providing, that lung cancer cells are</p> <p>2 irrelevant to the ovary in terms of study</p> <p>3 of this issue?</p> <p>4 MS. SHARKO: Object to the</p> <p>5 form of the question.</p> <p>6 THE WITNESS: Can you repeat</p> <p>7 the question? I'm not sure, there</p> <p>8 was a lot of --</p> <p>9 BY DR. THOMPSON:</p> <p>10 Q. Yeah, it was a bad -- it was</p> <p>11 a bad -- it was a bad question.</p> <p>12 A. Sorry.</p> <p>13 Q. Can you point me to an</p> <p>14 article that's on your reference list or</p> <p>15 materials considered list that addresses</p> <p>16 the basis for your opinion that lung</p> <p>17 cancer cells are irrelevant to ovarian</p> <p>18 cancer?</p> <p>19 A. I -- I didn't say lung</p> <p>20 cancer cells were irrelevant to ovarian</p> <p>21 cancer, although I would agree largely</p> <p>22 with that statement.</p> <p>23 What I said was lung cancer</p> <p>24 cells -- the use of lung cancer cells to</p>
<p style="text-align: right;">Page 407</p> <p>1 mutations. I believe it's -- it's either</p> <p>2 G12B or G12D, and that is completely</p> <p>3 irrelevant to the overwhelming majority</p> <p>4 of serous cancers, much less serous</p> <p>5 ovarian cancer transformation.</p> <p>6 So it's a lung epithelial</p> <p>7 cell. It's a transformed lung epithelial</p> <p>8 cell. It's bearing a mutation that is</p> <p>9 not found characteristically in serous</p> <p>10 cancer, and it's bearing a mutation that</p> <p>11 when it's found in serous cancer is not</p> <p>12 part of the initiating events in serous</p> <p>13 cancer.</p> <p>14 So irrelevant cell type,</p> <p>15 irrelevant mutations, irrelevant stage of</p> <p>16 carcinogenesis, and questionable dose.</p> <p>17 I -- I don't really see anything that</p> <p>18 could possibly be relevant to the</p> <p>19 question at hand when every other issue</p> <p>20 is irrelevant.</p> <p>21 Q. Is there any publication on</p> <p>22 your reference list or your materials</p> <p>23 considered list that would provide</p> <p>24 insight into that opinion that you're</p>	<p style="text-align: right;">Page 409</p> <p>1 determine the effects of agents on</p> <p>2 nontransformed ovarian epithelial cells</p> <p>3 or fallopian tube epithelial cells is</p> <p>4 irrelevant.</p> <p>5 And I think that should be</p> <p>6 self-evident to any practicing scientist</p> <p>7 in the cancer biology field. I don't</p> <p>8 think you would find any scientist,</p> <p>9 credible cancer biologist, who would</p> <p>10 think that using A-549 cells to model any</p> <p>11 aspect of ovarian cancer pathogenesis is</p> <p>12 relevant.</p> <p>13 Q. Well --</p> <p>14 A. And I would reject</p> <p>15 categorically from the six journals that</p> <p>16 I'm an editor of any paper that presumed</p> <p>17 to do the same, which is probably why a</p> <p>18 journal -- a paper like this is published</p> <p>19 in a low impact, low quality journal, and</p> <p>20 not in any of the six journals that I'm</p> <p>21 an editorial board member of or that I've</p> <p>22 been an editor of previously.</p> <p>23 Q. I understand that. But we</p> <p>24 have to be able to explain your opinions</p>

<p style="text-align: right;">Page 410</p> <p>1 to nonscientists. And it would be --</p> <p>2 will be helpful to be able to refer to an</p> <p>3 article or something that can address the</p> <p>4 irrelevance of -- of using these cell</p> <p>5 lines to study ovarian cancer</p> <p>6 pathogenesis.</p> <p>7 And my question is, is there</p> <p>8 a citation on your reference or materials</p> <p>9 cited -- materials considered list that</p> <p>10 we could refer to to help?</p> <p>11 MS. SHARKO: Object. Object</p> <p>12 to the form.</p> <p>13 THE WITNESS: I don't think</p> <p>14 I would have any trouble</p> <p>15 convincing anybody who is logical</p> <p>16 that studying a fully transformed</p> <p>17 lung cancer cell is not relevant</p> <p>18 to studying a normal fallopian</p> <p>19 tube cell.</p> <p>20 I think that stems from</p> <p>21 elemental logic and you don't</p> <p>22 really even have to have much</p> <p>23 scientific credentials to make</p> <p>24 that conclusion.</p>	<p style="text-align: right;">Page 412</p> <p>1 personal -- first of all, I heard</p> <p>2 that. And it's not a personal</p> <p>3 opinion.</p> <p>4 That is a scientific opinion</p> <p>5 based on 39 years of research, and</p> <p>6 I don't think you will ever find a</p> <p>7 credible scientific expert in the</p> <p>8 field of cancer biology who would</p> <p>9 say that studying A-549 in cancer</p> <p>10 cells from the lung is relevant to</p> <p>11 understanding the pathogenesis of</p> <p>12 fallopian tube and/or ovarian</p> <p>13 cancer. It's simply irrelevant.</p> <p>14 And, again, I can cite and</p> <p>15 did cite in my report the fact</p> <p>16 that high grade serous cancer is</p> <p>17 not categorized by KRAS mutations.</p> <p>18 These cells have KRAS mutations.</p> <p>19 Okay? I know that because we work</p> <p>20 with these cells in a different</p> <p>21 context.</p> <p>22 BY DR. THOMPSON:</p> <p>23 Q. So if there were a scientist</p> <p>24 that would give an opinion that there is</p>
<p style="text-align: right;">Page 411</p> <p>1 BY DR. THOMPSON:</p> <p>2 Q. So that opinion at least is</p> <p>3 based on logic, not peer-reviewed medical</p> <p>4 literature; is that correct?</p> <p>5 A. That -- that --</p> <p>6 MS. SHARKO: Object to the</p> <p>7 form. Misstates the testimony.</p> <p>8 THE WITNESS: That opinion</p> <p>9 is based on 39 years of experience</p> <p>10 in the cancer biology field from</p> <p>11 its earliest days. And from the</p> <p>12 general understanding of cell</p> <p>13 biology, molecular biology, and</p> <p>14 cancer biology that I and many</p> <p>15 other scientists of my credibility</p> <p>16 and credentials would hold.</p> <p>17 BY DR. THOMPSON:</p> <p>18 Q. As far as referring me to a</p> <p>19 citation in your report or attachments,</p> <p>20 that would address this issue, you are</p> <p>21 not able to do that today?</p> <p>22 MS. SHARKO: Objection.</p> <p>23 Asked and answered several times.</p> <p>24 THE WITNESS: That's not a</p>	<p style="text-align: right;">Page 413</p> <p>1 relevance to studying the effects of</p> <p>2 talcum powder or some other potential</p> <p>3 carcinogen on cell lines other than</p> <p>4 normal tubal primary cell lines, would</p> <p>5 you automatically have a criticism of</p> <p>6 that particular scientist?</p> <p>7 A. I would have to see the</p> <p>8 scientist's opinion in detail, but</p> <p>9 anybody who -- anybody with training in</p> <p>10 modern cancer biology and with an</p> <p>11 understanding that A-549 cells are lung</p> <p>12 epithelial, the adenocarcinoma cells that</p> <p>13 bear a KRAS mutation, and anyone who knew</p> <p>14 about the pathogenesis of high grade</p> <p>15 serous ovarian cancer would realize that</p> <p>16 that's not a relevant cell system.</p> <p>17 I would expect a first year</p> <p>18 graduate student to know that, frankly,</p> <p>19 and even a good undergraduate.</p> <p>20 Q. There are certain carcinogen</p> <p>21 that cause cancer in many different</p> <p>22 tissues and different types of cancer,</p> <p>23 aren't there?</p> <p>24 A. There are some carcinogens</p>

<p style="text-align: right;">Page 414</p> <p>1 that have the capacity to damage DNA in 2 many types of tissues, yes. 3 Q. And an example would be 4 asbestos, would it not? 5 A. As I said, I haven't really 6 exhaustively looked at the literature for 7 asbestos and cancer. But the only, you 8 know, thing that I know for sure is that 9 asbestos causes mesothelioma and is a 10 cocarcinogen with tobacco smoke for lung 11 cancer. 12 Q. So you are not aware of 13 other organs in which asbestos has been 14 shown to cause cancer as well? 15 A. I just said it's a cause of 16 mesothelioma. And it's a cocarcinogen 17 with tobacco smoke for lung epithelial 18 cancer. And there's some evidence it may 19 also cause lung epithelial cancer. 20 Q. And you have the IARC 2012 21 monograph on asbestos. Can you identify 22 the other types of cancer that IARC 23 concluded were caused by asbestos in 24 addition to mesothelioma?</p>	<p style="text-align: right;">Page 416</p> <p>1 developed cancer cells. 2 The question at hand, as I 3 understand the question, is does talc 4 contribute to the cause of ovarian 5 cancer. Once you have a fully -- fully 6 transformed lung cancer cell, it's a 7 cancer. 8 Q. But we have discussed 9 earlier that at least part of the 10 carcinogenic process includes promotion 11 and -- and progression of the cancer, 12 correct? 13 A. This cancer is a fully 14 developed, fully formed cancer. It's 15 gone way behind the progression and 16 initiation stages. This cancer will kill 17 a mouse if you inject it into a mouse. 18 It's not -- it's not a precancerous 19 lesion. It's not a cancer -- it's not a 20 lesion that it is in the process of 21 carcinogenesis. It's fully blown lung 22 cancer cell line derived probably from a 23 metastatic lung cancer patient who 24 underwent surgery. So it -- it's really</p>
<p style="text-align: right;">Page 415</p> <p>1 A. I -- 2 MS. SHARKO: Object to the 3 form. 4 THE WITNESS: I said that I 5 haven't really studied the IARC 6 monograph, so I can't comment on 7 that. 8 BY DR. THOMPSON: 9 Q. And would anyone who relies 10 on studies looking at the cell lines that 11 you've been discussing, that you deem 12 irrelevant, would they be wrong for doing 13 so? 14 A. I didn't say that the cell 15 lines were irrelevant. I said the cell 16 lines were irrelevant to the question at 17 hand. 18 These cell lines are highly 19 relevant to understanding lung cancer 20 pathogenesis. But they are not relevant 21 to understanding ovarian cancer 22 pathogenesis. 23 Q. Okay. Sir -- 24 A. And these cells are fully</p>	<p style="text-align: right;">Page 417</p> <p>1 not relevant in my opinion. 2 Q. Okay. 3 (Document marked for 4 identification as Exhibit 5 Neel-33.) 6 BY DR. THOMPSON: 7 Q. I'm going to give you 8 another paper by the -- at least Akhtar 9 is the same. 10 This is Exhibit 33, Akhtar, 11 "Cytotoxicity and apoptosis induction by 12 nanoscale talc particles." 13 Have you seen this paper, 14 Dr. Neel? 15 A. 70 and 71, that must be -- 16 Q. Oh, that's the -- 17 A. Let me see if that's the 18 paper that I cited. It's -- 19 MS. SHARKO: Yes. 20 THE WITNESS: Yeah, I've 21 seen this paper. I refer to it in 22 my report. It's in the context of 23 the same issues that we just 24 discussed.</p>

<p style="text-align: right;">Page 418</p> <p>1 BY DR. THOMPSON:</p> <p>2 Q. And are your criticisms of</p> <p>3 this paper similar to the other Akhtar</p> <p>4 paper?</p> <p>5 A. Yes, it -- yes, again uses a</p> <p>6 single lung cancer cell line which is</p> <p>7 fully transformed and bears KRAS</p> <p>8 mutations and, therefore, is not relevant</p> <p>9 to nontransformed fallopian tube</p> <p>10 epithelium or ovarian surface epithelium.</p> <p>11 Nor is it relevant to serous cancer</p> <p>12 pathogenesis because serous cancers</p> <p>13 almost never have KRAS mutations, and</p> <p>14 when they do have KRAS mutation, they are</p> <p>15 a later stage of development and are not</p> <p>16 involved in the initial stages of cancer.</p> <p>17 That is well established</p> <p>18 from modern molecular biology research.</p> <p>19 Q. And this paper was peer</p> <p>20 reviewed and published, correct?</p> <p>21 A. I assume so. What journal</p> <p>22 is this? I don't even know what</p> <p>23 journal -- I assume it was.</p> <p>24 Q. And the authors at least</p>	<p style="text-align: right;">Page 420</p> <p>1 of this paper are pretty much the same as</p> <p>2 the criticisms I have with the other</p> <p>3 Akhtar paper. Irrelevant cell line,</p> <p>4 uncertain dose. You know, no</p> <p>5 demonstration. We -- they couldn't</p> <p>6 actually demonstrate carcinogenesis here</p> <p>7 because they start with a cancer.</p> <p>8 Q. Would you say that all four</p> <p>9 of these molecular studies relating to</p> <p>10 talc are flawed in some way?</p> <p>11 A. I only count two.</p> <p>12 MS. SHARKO: Object. Object</p> <p>13 to the form.</p> <p>14 THE WITNESS: We're only</p> <p>15 discussing two.</p> <p>16 BY DR. THOMPSON:</p> <p>17 Q. Oh, I'm including Buz'Zard</p> <p>18 and Shukla.</p> <p>19 A. Oh yes, they are all</p> <p>20 completely flawed from the standpoint of</p> <p>21 the question at hand, yes. They are not</p> <p>22 even close to being on point in my</p> <p>23 opinion, professional opinion, based on</p> <p>24 39 years of research in cancer biology</p>
<p style="text-align: right;">Page 419</p> <p>1 concluded that the particles that they</p> <p>2 used which were commercial -- indigenous</p> <p>3 and commercial nano talc particles,</p> <p>4 right?</p> <p>5 A. That is what they say, yes.</p> <p>6 Q. Okay. And the authors at</p> <p>7 least conclude that the particles</p> <p>8 significantly induced cytotoxicity,</p> <p>9 oxidative stress and apoptosis in human</p> <p>10 lung epithelial cells?</p> <p>11 A. Well, first of all, they are</p> <p>12 not human lung epithelial cells. As I</p> <p>13 said that's a misstatement. They are</p> <p>14 human lung cancer cells.</p> <p>15 So the title is misleading.</p> <p>16 And that conclusion is misleading.</p> <p>17 Human lung epithelial cells</p> <p>18 can -- would normally be interpreted as,</p> <p>19 say, normal human lung epithelial cells.</p> <p>20 So these are human lung cancer cells.</p> <p>21 That would be a more accurate statement.</p> <p>22 Q. Do you have other criticisms</p> <p>23 of the -- this paper?</p> <p>24 A. The criticisms that I have</p>	<p style="text-align: right;">Page 421</p> <p>1 dating from the -- from the earliest days</p> <p>2 of the field and staying current in</p> <p>3 modern molecular biology research.</p> <p>4 DR. THOMPSON: Would this be</p> <p>5 a good time for a break?</p> <p>6 MS. SHARKO: Again?</p> <p>7 DR. THOMPSON: How long has</p> <p>8 it been?</p> <p>9 MS. O'DELL: A little over</p> <p>10 an hour. I think it's an</p> <p>11 appropriate time for a break.</p> <p>12 THE VIDEOGRAPHER: Remove</p> <p>13 your microphones. The time is</p> <p>14 5:03 p.m. Off the record.</p> <p>15 (Short break.)</p> <p>16 THE VIDEOGRAPHER: Okay. We</p> <p>17 are back on the record. The time</p> <p>18 is 5:24 p.m.</p> <p>19 BY DR. THOMPSON:</p> <p>20 Q. Dr. Neel, we've looked at</p> <p>21 five molecular studies this afternoon.</p> <p>22 That paper by Saed, by Shukla, Buz'Zard,</p> <p>23 and two by Akhtar.</p> <p>24 Is it your opinion that all</p>

<p style="text-align: right;">Page 422</p> <p>1 five of those studies are flawed?</p> <p>2 A. They are either flawed or</p> <p>3 they are not relevant.</p> <p>4 Q. And the -- the reason for</p> <p>5 that criticism seems to be primarily that</p> <p>6 there is no established dose and that the</p> <p>7 wrong cell lines are used. Is that a</p> <p>8 fair statement?</p> <p>9 A. That is --</p> <p>10 MS. SHARKO: Object to the</p> <p>11 form.</p> <p>12 THE WITNESS: That statement</p> <p>13 refers to some of the papers. But</p> <p>14 Dr. Saed's paper is flawed on</p> <p>15 multiple levels, most notably his</p> <p>16 claim that talc applied to ovarian</p> <p>17 cells or fallopian tube cells can</p> <p>18 produce a stoichiometric shift in</p> <p>19 nucleotide sequence for a specific</p> <p>20 gene. That is just an incredible</p> <p>21 assertion.</p> <p>22 So -- and also his claims</p> <p>23 that redox balance is disrupted in</p> <p>24 the cells without any measurement</p>	<p style="text-align: right;">Page 424</p> <p>1 BY DR. THOMPSON:</p> <p>2 Q. Sure.</p> <p>3 A. She distracted me. Sorry.</p> <p>4 Q. So --</p> <p>5 MS. SHARKO: Sorry, that was</p> <p>6 not my intention.</p> <p>7 BY DR. THOMPSON:</p> <p>8 Q. So is it your opinion that</p> <p>9 any scientist who relied on those studies</p> <p>10 to formulate their opinions as to whether</p> <p>11 talcum powder use could cause ovarian</p> <p>12 cancer, would be using poor judgment from</p> <p>13 a scientific standpoint?</p> <p>14 A. Yes. I would have to say</p> <p>15 that.</p> <p>16 Q. And would it be your opinion</p> <p>17 that any scientist who relied on those</p> <p>18 studies to answer the question of whether</p> <p>19 talcum powder use could cause ovarian</p> <p>20 cancer, would not have a sufficient</p> <p>21 understanding of molecular and cellular</p> <p>22 biology?</p> <p>23 A. If that's the basis for</p> <p>24 their opinion, then they are not -- yes,</p>
<p style="text-align: right;">Page 423</p> <p>1 of redox balance in the cells.</p> <p>2 You can't make that claim without</p> <p>3 actually measuring redox balance.</p> <p>4 So his paper, the -- the one</p> <p>5 that's in -- that just was</p> <p>6 published apparently is flawed</p> <p>7 conceptually and technically.</p> <p>8 The other papers are using</p> <p>9 questionable doses and irrelevant</p> <p>10 cell systems. So they're</p> <p>11 different objections to the</p> <p>12 different studies.</p> <p>13 BY DR. THOMPSON:</p> <p>14 Q. So is it your opinion that</p> <p>15 any scientist who relies on these studies</p> <p>16 would be using -- relying on these</p> <p>17 studies to answer the question of whether</p> <p>18 talcum powder causes ovarian cancer,</p> <p>19 would be using bad scientific judgment?</p> <p>20 MS. SHARKO: Object to the</p> <p>21 form of the question.</p> <p>22 THE WITNESS: What -- what</p> <p>23 would -- can you repeat the</p> <p>24 question?</p>	<p style="text-align: right;">Page 425</p> <p>1 that would be my opinion.</p> <p>2 Q. Would -- would you look at</p> <p>3 your CV which is exhibit -- something not</p> <p>4 very high.</p> <p>5 A. Yes. I have it.</p> <p>6 Q. Okay. And before we get to</p> <p>7 your CV, was -- would it be your opinion</p> <p>8 that any scientist who relies on these</p> <p>9 studies for opinions on the biological</p> <p>10 plausibility of talcum powder use causing</p> <p>11 ovarian cancer to be using poor</p> <p>12 scientific judgment?</p> <p>13 MS. SHARKO: I object to the</p> <p>14 form of the question. Can you</p> <p>15 break it down by study?</p> <p>16 MS. O'DELL: No.</p> <p>17 THE WITNESS: So if the --</p> <p>18 if the only studies that they used</p> <p>19 to reach the opinion that talc</p> <p>20 caused ovarian cancer were these</p> <p>21 five highly flawed studies, they</p> <p>22 would be exercising poor</p> <p>23 scientific judgment in my opinion.</p> <p>24 BY DR. THOMPSON:</p>

1 Q. Even on biological
2 plausibility?

3 A. Oh, for sure, yes. I don't
4 think these -- these papers are credible
5 assessments of biologic plausibility at
6 all in any way.

7 Q. And if the scientists who
8 rely on these studies for their opinions
9 regarding the biological plausibility of
10 talcum powder use causing ovarian cancer
11 would also not have a sufficient
12 understanding of molecular cellular
13 biology?

14 MS. SHARKO: Object to the
15 form of the question.

16 THE WITNESS: I -- I think
17 that it would depend on what --
18 they might have an understanding
19 of some aspects of cell and
20 molecular biology. But they would
21 not have any understanding of
22 other aspects of cellular and
23 molecular biology. So that's a
24 very difficult question to answer.

1 If you ask a more specific
2 question, I can help you with an
3 answer.

4 BY DR. THOMPSON:

5 Q. But at least the opinions
6 relating to the biological plausibility
7 for that, to answer that question, their
8 understanding in your opinion would be
9 inadequate?

10 A. I think that someone who
11 read these papers and thought that they
12 provided plausibility for the contention
13 that talc causes ovarian cancer would
14 have poor scientific judgment as to that
15 question, yes.

16 Q. Let's go ahead and look at
17 your CV now.

18 A. Sure.

19 Q. And we'll do the same thing
20 we did before. So using your criteria of
21 an established dose, an appropriate cell
22 line, are there any of your publications
23 that you think are relevant to the
24 question as to whether talcum powder

1 products can cause ovarian cancer?

2 A. No. As I've said before, I
3 haven't studied that issue and I wouldn't
4 be able to study that issue in my current
5 position.

6 Q. Okay. Have you ever
7 published in Gynecologic Oncology, to
8 your knowledge?

9 A. I may have been a co-author
10 on a paper in Gynecologic Oncology. But
11 I have not been a senior author on any
12 paper in Gynecologic Oncology.

13 Q. Should any study that treats
14 ovarian cancer as a single entity be used
15 with skepticism?

16 A. I think today, yes.

17 Q. Is this because ovarian
18 cancer is not a single disease?

19 A. Yes.

20 Q. But isn't hormone -- hormone
21 responsiveness a common link among all
22 ovarian cancer subtypes?

23 A. Hormone responsive -- the
24 endometrioid and clear cell cases are

1 much more clearer about hormone
2 responsiveness. Whether serous cancers
3 are hormone responsive probably -- it
4 depends on the cancer.

5 So -- and whether it's
6 involved in pathogenesis is also not as
7 well established.

8 Q. But at least some scientists
9 would argue that hormone responsiveness
10 would be one of those factors that could
11 cross all histologic subtypes?

12 A. Again, I can't comment on
13 specific -- on general statements like
14 some scientists. If you give me a
15 specific statement that was made by a
16 specific scientist, I can look at it and
17 I can determine whether I agree with it
18 or not or whether I think it's credible.

19 Q. Has it been published that
20 hormone responsiveness would be a factor
21 that would cross all subtypes to your
22 knowledge?

23 A. There have been -- there --
24 there have been reports that hormone

<p style="text-align: right;">Page 430</p> <p>1 replacement therapy may be oncogenic, you 2 know, procarcinogenic in ovarian cancer. 3 Q. And that includes all 4 subtypes? 5 A. Well, the effects are much 6 stronger for, as I said clear cell and 7 endometrial cancers. And whether it's 8 true for high grade serous is less clear, 9 from my -- from my recollection of the 10 literature. 11 Q. Could a reasonable scientist 12 discuss ovarian breast cancer and 13 endometriosis as a group because they are 14 all hormonally responsive lesions? 15 MS. SHARKO: Object to the 16 form of the question. 17 THE WITNESS: Discuss in 18 what context? I don't understand 19 the question. 20 MS. SHARKO: You can ask 21 them to read their handwriting. 22 BY DR. THOMPSON: 23 Q. If you were looking at in 24 vitro studies, would it be appropriate to</p>	<p style="text-align: right;">Page 432</p> <p>1 Q. Has that been studied? 2 A. I don't know the answer to 3 that question, so I would be 4 uncomfortable answering it. 5 Q. Could a reasonable scientist 6 make that statement? 7 A. I don't know. I'd have to 8 see the paper. I'm happy to look at the 9 paper and go over the data if there is 10 such a paper. 11 Q. Could inflammation-induced 12 proliferation in the tubal epithelium, in 13 the epithelial, if that did occur, 14 progress to papillary tubal hyperplasia? 15 A. What do you mean by 16 papillary tubal hyperplasia? Do you mean 17 STICs? 18 Q. Let's say STICs. 19 A. I don't know. I'd have 20 to -- I'd have to see the study. I'm not 21 going to speculate on mechanisms that I 22 haven't seen in the -- in the press -- in 23 the scientific press. 24 Q. In addition to the Saed</p>
<p style="text-align: right;">Page 431</p> <p>1 use either serous breast or endometrioid 2 cancer cell lines and extrapolate the 3 information from one to the other? 4 A. What's the question? Not 5 what's your question, but what's the 6 scientific question that's being asked? 7 I mean, if you want to just look at 8 hormone responsive gene expression, then 9 maybe. If the question is having to do 10 with the pathogenesis of each of the 11 individual diseases, then probably not. 12 It would depend on the 13 specifics though. Scientists don't think 14 that way. They think in very specific 15 terms so they can frame accurate 16 questions that can yield results that are 17 interpretable. So I can't answer a 18 question that's so generic and 19 nonspecific as that. 20 Q. Can chronic inflammation 21 induce a proliferation of tubal 22 epithelium? 23 A. I don't know the answer to 24 that question.</p>	<p style="text-align: right;">Page 433</p> <p>1 papers that you did not list in the 2 materials considered or the supplemental 3 materials, are there any other papers 4 that were -- that form the basis of your 5 criticisms of either the Saed or the 6 other molecular papers? 7 MS. SHARKO: Object to the 8 form of the question. Lacks 9 foundation. 10 THE WITNESS: I think you 11 misunderstood or maybe I was 12 unclear before. 13 My opinion of the Saed paper 14 that was just published is based 15 on the Saed paper that was just 16 published. 17 And that doesn't need me to 18 read any of his earlier papers. 19 My comments about some of 20 his earlier papers had -- went to 21 the issue of erroneous statements 22 that were made in his report. 23 Having to do, for example, with 24 the expression of myeloperoxidase</p>

Page 434	Page 436
<p>1 and ovarian cancer cells, having 2 to do with the statement that p53 3 is an oncogene, whereas it's a 4 paradigmatic tumor suppressor 5 gene, having to do with statements 6 regarding SNPs that are not in the 7 GWAS catalogue of well-recognized 8 ovarian cancer SNPs.</p> <p>9 But that had nothing to do 10 with my criticisms of his paper, 11 which stand independent of any 12 other issues regarding Dr. Saed's 13 qualifications or expertise.</p> <p>14 DR. THOMPSON: Object as 15 nonresponsive.</p> <p>16 BY DR. THOMPSON:</p> <p>17 Q. Because my question was 18 really only, are there any other papers 19 or literature that form the basis?</p> <p>20 A. With respect, DR. THOMPSON, 21 the question that you asked me, as I 22 understand it, and you're welcome to read 23 it back to me, but I believe your 24 question was, were there any other papers</p>	<p>1 clarify, were there -- the papers that 2 you considered informing those opinions 3 regarding Dr. Saed that you have not 4 mentioned so far?</p> <p>5 A. No.</p> <p>6 Q. Okay. Have you sent any 7 comments to Health Canada?</p> <p>8 A. No.</p> <p>9 Q. Do you plan to send any 10 comments to Health Canada?</p> <p>11 A. I don't know if it's 12 appropriate for me to send any comments 13 to Health Canada while I'm involved in 14 this litigation. I would have to consult 15 Ms. Sharko and Mr. Zellers as to whether 16 I should.</p> <p>17 Q. You'll agree that talc and 18 its potential contribution to ovarian 19 cancer has been an issue for several 20 decades. Would you agree with that, in 21 the literature?</p> <p>22 A. It's certainly been in the 23 epidemiological literature. In the 24 biology literature, there's actually</p>
Page 435	Page 437
<p>1 that led to my objection to his, you 2 know, paper in Reproductive Biology.</p> <p>3 And the answer to that is 4 none of those other papers are directly 5 relevant to the paper in Reproductive 6 Biology. The errors in the paper of 7 Reproductive Biology stand on their own 8 and are clearly determinable by anyone 9 with expertise in modern cellular and 10 molecular biology.</p> <p>11 MS. SHARKO: Okay. I think 12 it's late. I think she's just 13 asking you if there are any papers 14 that you're relying on that aren't 15 listed in the report and reliance 16 materials.</p> <p>17 THE WITNESS: No.</p> <p>18 BY DR. THOMPSON:</p> <p>19 Q. And Ms. Sharko is correct. 20 That was the question that I was trying 21 to ask.</p> <p>22 A. Okay. And that question is 23 no.</p> <p>24 Q. And I'm just going to</p>	<p>1 relatively limited studies, which is why 2 we've been actually able to cover most of 3 them in this last hour or two.</p> <p>4 Q. And that would be for talc, 5 but certainly there have been studies 6 regarding the molecular basis for 7 asbestos and it's carcinogenic potential, 8 correct?</p> <p>9 A. As I said, I haven't done an 10 exhaustive study of what's in the 11 literature about asbestos and its role in 12 ovarian cancer. I think you asked me 13 about talc, which is what I answered.</p> <p>14 Q. I asked you about talcum 15 powder. Or I meant to ask about talcum 16 powder.</p> <p>17 A. Yes. And I answered that.</p> <p>18 Q. Have you ever been asked to 19 do an in vitro study with talcum powder?</p> <p>20 A. No.</p> <p>21 Q. Have you ever been asked to 22 do an in vivo study with talcum powder?</p> <p>23 A. No.</p> <p>24 Q. And could you do either an</p>

<p style="text-align: right;">Page 438</p> <p>1 in vitro study or an in vivo study to 2 evaluate the causal connection between 3 talcum powder or the potential causal 4 connection between talcum powder and 5 ovarian cancer? 6 A. Not in my -- 7 MS. SHARKO: Objection. 8 Asked and answered a zillion 9 times. 10 THE WITNESS: I'll -- 11 that's -- 12 BY DR. THOMPSON: 13 Q. This question -- sorry. 14 This question is outside the context of 15 your current situation. 16 Could you do that study? 17 A. Could I do the study? I 18 would have to really seriously think 19 about the problem and then decide whether 20 I could do a good study. There would be 21 several problems, many of which I've 22 already described, having to do with 23 coming to arrive at a reasonable dose. I 24 probably could test a range of doses in a</p>	<p style="text-align: right;">Page 440</p> <p>1 and more physiologically relevant 2 systems than, for example, 3 Dr. Saed did, and certainly the 4 other four papers which were off 5 point in my opinion. 6 DR. THOMPSON: I have no 7 further questions. 8 MS. SHARKO: Okay. We're 9 done. Thank you very much. 10 THE WITNESS: Thank you. 11 THE VIDEOGRAPHER: Okay. 12 Stand by, please. This marks the 13 end of today's deposition. The 14 time is 5:42 p.m. 15 (Excused.) 16 (Deposition concluded at 17 approximately 5:42 p.m.) 18 19 20 21 22 23 24</p>
<p style="text-align: right;">Page 439</p> <p>1 biologically relevant system than, for 2 example, any of the five papers that we 3 discussed extensively in the last two 4 hours did. 5 Q. So at least today, sitting 6 here, you're not sure whether you could 7 do the quality study that would be 8 required or not; is that fair? 9 MS. SHARKO: Object to the 10 form. 11 THE WITNESS: I'm saying 12 that it's not clear that enough 13 information is available to design 14 a study, not that I couldn't do 15 it. I could certainly do it if a 16 reasonable -- if there were clear 17 information about a dose range of 18 talc that was in -- if there were 19 talc in fallopian tube and/or 20 there were talc in ovarian 21 adnexa -- in the adnexa -- in the 22 ovarian surface endothelium or 23 region, I could do a reasonable 24 study using those doses of talc</p>	<p style="text-align: right;">Page 441</p> <p>1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24</p> <p style="text-align: center;">CERTIFICATE</p> <p>I HEREBY CERTIFY that the witness was duly sworn by me and that the deposition is a true record of the testimony given by the witness.</p> <p>It was requested before completion of the deposition that the witness, BENJAMIN G. NEEL, M.D., Ph.D., have the opportunity to read and sign the deposition transcript.</p> <hr/> <p>MICHELLE L. GRAY, A Registered Professional Reporter, Certified Shorthand Reporter, Certified Realtime Reporter and Notary Public Dated: March 20, 2019</p> <p>(The foregoing certification of this transcript does not apply to any reproduction of the same by any means, unless under the direct control and/or supervision of the certifying reporter.)</p>

Benjamin G. Neel, M.D., Ph.D.

Page 442

INSTRUCTIONS TO WITNESS

Please read your deposition over carefully and make any necessary corrections. You should state the reason in the appropriate space on the errata sheet for any corrections that are made.

After doing so, please sign the errata sheet and date it.

You are signing same subject to the changes you have noted on the errata sheet, which will be attached to your deposition.

It is imperative that you return the original errata sheet to the depositing attorney within thirty (30) days of receipt of the deposition transcript by you. If you fail to do so, the deposition transcript may be deemed to be accurate and may be used in court.

Page 444

ACKNOWLEDGMENT OF DEPONENT

I, _____, do hereby certify that I have read the foregoing pages, 1 - 445, and that the same is a correct transcription of the answers given by me to the questions therein propounded, except for the corrections or changes in form or substance, if any, noted in the attached Errata Sheet.

BENJAMIN G. NEEL, M.D., Ph.D. DATE

Subscribed and sworn to before me this

_____ day of _____, 20_____.

My commission expires: _____

Notary Public

Page 443

E R R A T A**PAGE LINE CHANGE**

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Page 445

LAWYER'S NOTES**PAGE LINE**

Exhibit 11

Gregory B. Diette, M.D.

Page 1

UNITED STATES DISTRICT COURT

DISTRICT OF NEW JERSEY

-----x

IN RE JOHNSON & JOHNSON) MDL No.
TALCUM POWDER PRODUCTS) 16-2738 (FLW)(LHG)
MARKETING SALES PRACTICES,)
AND PRODUCTS LIABILITY)
LITIGATION)
)
THIS DOCUMENT RELATES TO)
ALL CASES)

-----x

VIDEOTAPED DEPOSITION OF

GREGORY B. DIETTE, M.D.

TOWSON, MARYLAND

TUESDAY, APRIL 9, 2019

8:58 A.M.

Reported by: Leslie A. Todd

Gregory B. Diette, M.D.

Page 2	Page 4
<p>1 Deposition of GREGORY B. DIETTE, M.D., held at 2 the: 3 4 5 SHERATON BALTIMORE NORTH HOTEL 6 903 Dulaney Valley Road 7 Towson, Maryland 21204 8 9 10 11 12 13 14 15 16 Pursuant to notice, before Leslie Anne Todd, 17 Court Reporter and Notary Public of the State of 18 Maryland, who officiated in administering the oath 19 to the witness. 20 21 22 23 24 25</p>	<p>1 APPEARANCES (Continued): 2 3 CYNTHIA L. GARBER, ESQUIRE 4 ROBINSON CALCAGNIE, INC 5 19 Corporate Plaza Drive 6 Newport Beach, California 92660 7 (949) 720-1288 8 9 NATHAN D. FINCH, ESQUIRE 10 MOTLEY RICE LLC 11 401 9th Street, NW 12 Suite 1001 13 Washington, D.C. 20004 14 (202) 232-5507 15 16 ON BEHALF OF THE JOHNSON & JOHNSON DEFENDANTS: 17 ALLISON M. BROWN, ESQUIRE 18 RICHARD M. HEASLIP, ESQUIRE 19 WEIL, GOTSHAL & MANGES LLP 20 17 Hutfish Street, Suite 201 21 Princeton, New Jersey 08542-3792 22 (609) 986-1104 23 24 25</p>
Page 3	Page 5
<p>1 A P P E A R A N C E S 2 3 ON BEHALF OF THE PLAINTIFFS: 4 MICHELLE PARFITT, ESQUIRE 5 ADAM K. ROSEN, ESQUIRE 6 ASHCRAFT & GEREL, LLP 7 1825 K Street, N.W. 8 Suite 700 9 Washington, D.C. 20006 10 (202) 783-6400 11 12 CHRISTOPHER V. TISI, ESQUIRE 13 LEVIN PAPANTONIO THOMAS MITCHELL 14 RAFFERTY PROCTOR, P.A. 15 316 South Baylen Street 16 Pensacola, Florida 32502 17 (850) 435-7000 18 19 DENNIS M. GEIER, ESQUIRE 20 COHEN PLACITELLA ROTH, PC 21 127 Maple Avenue 22 Red Bank, New Jersey 07701 23 (732) 747-9003 24 25</p>	<p>1 APPEARANCES (Continued): 2 3 KATHERINE MCBETH, ESQUIRE 4 DRINKER BIDDLE & REATH, LLP 5 One Logan Square, Suite 2000 6 Philadelphia, Pennsylvania 19103-69896 7 (215) 988-2706 8 9 JESSICA D. MILLER, ESQUIRE 10 SKADDEN, ARPS, MEAGHER & FLOM, LLP 11 1440 New York Avenue, N.W. 12 Washington, D.C. 20005 13 (202) 371-7000 14 15 ON BEHALF OF THE PCPC: 16 THOMAS T. LOCKE, ESQUIRE 17 SEYFARTH SHAW LLP 18 975 F Street, N.W. 19 Washington, D.C. 20004-1454 20 (202) 463-2400 21 22 ALSO PRESENT: 23 DANIEL HOLMSTOCK, Videographer 24 25</p>

2 (Pages 2 to 5)

Gregory B. Diette, M.D.

Page 6			Page 8		
1	CONTENTS		1	EXHIBITS (Continued)	
2	EXAMINATION OF GREGORY B. DIETTE, M.D.	PAGE	2	(Attached to transcript)	
3	By Ms. Parfitt	14	3	DIETTE DEPOSITION EXHIBITS	PAGE
4	By Mr. Finch	465	4	No. 13 Document headed "Statement of Dr.	
5	By Ms. Brown	467	5	Anne Mc Tiernan prepared for the	
6			6	Subcommittee on Economic and	
7			7	Consumer Policy Hearing on Examining	
8	EXHIBITS		8	the Public Health Risk on	
9	(Attached to transcript)		9	Carcinogens and Consumer Products,	
10	DIETTE DEPOSITION EXHIBITS	PAGE	10	March 12, 2019"	235
11	No. 1 Notice of Oral and Videotaped		11	No. 14 Draft Screening Assessment, Talc,	
12	Deposition of Gregory Diette, MD,		12	Chemical Abstracts Service Registry	
13	MHS, and Duces Tecum	16	13	Number 14807-96-6, Environment and	
14	No. 2 Defendants' Response to Plaintiffs'		14	Climate Change Canada, Health Canada,	
15	Document Requests Contained in Notice		15	December 2018	267
16	of Oral and Videotaped Deposition of		16	No. 15 Article entitled "Asbestos Exposure	
17	Gregory Diette, M.D., MHS and Duces		17	and Ovarian Fiber Burden," Bates	
18	Tecum	17	18	JNJ 000004999 to 000005003	281
19	No. 3 Expert Report of Gregory Diette, MD,		19	No. 16 Excerpt from "Modern Epidemiology,"	
20	MHS for General Causation Daubert		20	Third Edition, by Rothman, Greenland	
21	Hearing, Supplemental Materials		21	and Lash	289
22	Reviewed and Considered	18	22	No. 17 Taylor and Francis Group article,	
23	No. 4 Article entitled "Ovulation and Risk		23	"Moving to a World Beyond "p < 0.05" 297	
24	of Epithelial Ovarian Cancer"	44	24		
25			25		

Page 7			Page 9		
1	EXHIBITS (Continued)		1	EXHIBITS (Continued)	
2	(Attached to transcript)		2	(Attached to transcript)	
3	DIETTE DEPOSITION EXHIBITS	PAGE	3	DIETTE DEPOSITION EXHIBITS	PAGE
4	No. 5 Bottle of Johnson's Baby Powder		4	No. 18 Article entitled "Retire statistical	
5	(Retained by Plaintiffs' Counsel)	52	5	Significance," by Amrhein, Greenland,	
6	No. 6 Excerpt of Deposition of Susan		6	McShane	299
7	Nicholson, M.D.	82	7	No. 19 Article from Johns Hopkins Institute	
8	No. 7 Document entitled "Appendix C"		8	for Clinical & Translational Research,	
9	Curriculum Vitae of Gregory B.		9	"The American Statistician Special	
10	Diette, MD, MHS	91	10	Issue: Moving to a World Beyond 'P	
11	No. 8 Document from Johns Hopkins Medicine		11	< 0.05'"	308
12	website, entitled "Find an Expert,"		12	No. 20 Supplementary information to: Retire	
13	Gregory Bruce Diette, M.D.	95	13	Statistical significance, Valentin	
14	No. 9 Gregory B. Diette, MD, Associate		14	Amrhein et al.	312
15	Professor, Departmental Affiliations	98	15	No. 21 Document entitled "Gregory Diette,	
16	No. 10 Expert Report of Gregory Diette, MD,		16	MD, MHS: Talc/Ovarian Cancer Disease	
17	MHS for General Causation Daubert		17	Control Studies (Hospital Studies	
18	Hearing	133	18	Below Line)	324
19	No. 11 Document entitled "Appendix E,"		19	No. 22 Chart showing Estimated Relative	
20	Expert Testimony of Gregory B.		20	Risk of Ovarian Cancer, According	
21	Diette, MD, MHS	138	21	to Reported Use of Talc, Bates	
22	No. 12 Document from the Sidney Kimmel		22	JNJ 000013131	327
23	Comprehensive Cancer Center, Risk		23		
24	Factors & Symptoms	213	24		
25			25		

3 (Pages 6 to 9)

Gregory B. Diette, M.D.

Page 10	Page 12
<p>1 EXHIBITS (Continued)</p> <p>2 (Attached to transcript)</p> <p>3 DIETTE DEPOSITION EXHIBITS PAGE</p> <p>4 No. 23 Article entitled "Exposure to</p> <p>5 Secondhand Smoke and Risk of Cancer</p> <p>6 in Never Smokers: A Meta-Analysis of</p> <p>7 Epidemiologic Studies" 366</p> <p>8 No. 24 International Journal of Cardiology</p> <p>9 article, "Risk of all-cause mortality</p> <p>10 and cardiovascular disease associated</p> <p>11 with secondhand smoke exposure: A</p> <p>12 systematic review and meta-analysis" 369</p> <p>13 No. 25 NIH Public Access Author Manuscript,</p> <p>14 "Common Household Activities are</p> <p>15 Associated with Elevated Particulate</p> <p>16 Matter Concentrations in Bedrooms of</p> <p>17 Inner-City Baltimore Pre-School</p> <p>18 Children" 377</p> <p>19 No. 26 "The Health Consequences of</p> <p>20 Involuntary Exposure to Tobacco</p> <p>21 Smoke," A Report of the Surgeon</p> <p>22 General 377</p> <p>23 No. 27 IARC Monograph entitled "Arsenic,</p> <p>24 Metals, Fibres and Dusts," Volume</p> <p>25 100 C, A review of Human Carcinogens 392</p>	<p>1 EXHIBITS (Continued)</p> <p>2 (Attached to transcript)</p> <p>3 DIETTE DEPOSITION EXHIBITS PAGE</p> <p>4 No. 34 Article entitled "Possible Role of</p> <p>5 Epithelial Inflammation in Ovarian</p> <p>6 Cancer" 442</p> <p>7</p> <p>8</p> <p>9</p> <p>10</p> <p>11</p> <p>12</p> <p>13</p> <p>14</p> <p>15</p> <p>16</p> <p>17</p> <p>18</p> <p>19</p> <p>20</p> <p>21</p> <p>22</p> <p>23</p> <p>24</p> <p>25</p>
Page 11	Page 13
<p>1 EXHIBITS (Continued)</p> <p>2 (Attached to transcript)</p> <p>3 DIETTE DEPOSITION EXHIBITS PAGE</p> <p>4 No. 28 Table 2.8 Epidemiologic studies of</p> <p>5 asbestos exposure and ovarian cancer</p> <p>6 (and, for comparison, lung cancer</p> <p>7 and mesothelioma) 396</p> <p>8 No. 29 Article entitled "Association between</p> <p>9 Body Powder Use and Ovarian Cancer:</p> <p>10 The African American Cancer</p> <p>11 Epidemiology Study (AACES)" 413</p> <p>12 No. 30 Article entitled "Perineal Talc Use</p> <p>13 and Ovarian Cancer, A Systematic</p> <p>14 Review and Meta-Analysis" 416</p> <p>15 No. 31 Ultrastructural Pathology article,</p> <p>16 "Correlative polarizing light and</p> <p>17 scanning electron microscopy for</p> <p>18 the assessment of talc in pelvic</p> <p>19 region lymph nodes" 427</p> <p>20 No. 32 Letter to Samuel Epstein from the</p> <p>21 Department of Health and Human</p> <p>22 Services, dated April 1, 2014 431</p> <p>23 No. 33 Facsimile dated September 30,</p> <p>24 2004 to Luzenac America from</p> <p>25 Richard Zazenski to Bill Ashton 437</p>	<p>1 PROCEEDINGS</p> <p>2 -----</p> <p>3 THE VIDEOGRAPHER: We are now on the</p> <p>4 record, and my name is Daniel Holmstock. I am the</p> <p>5 videographer for Golkow Litigation Services.</p> <p>6 Today's date is April 9th, 2019, and the time on</p> <p>7 the video screen is 8:58 a.m.</p> <p>8 This video deposition is being held at</p> <p>9 the Sheraton Baltimore North Hotel, at 903 Dulaney</p> <p>10 Valley Road in Towson, Maryland, in the matter of</p> <p>11 Johnson & Johnson Talcum Powder Products</p> <p>12 Marketing, Sales Practices and Products Liability</p> <p>13 Litigation, MDL No. 2738, and is pending before</p> <p>14 the United States District Court for the Eastern</p> <p>15 District of New Jersey.</p> <p>16 Our deponent today is Dr. Gregory</p> <p>17 Diette.</p> <p>18 Counsel for appearances will be noted on</p> <p>19 the stenographic record. And our court reporter</p> <p>20 today is Leslie A. Todd, who will now administer</p> <p>21 the oath.</p> <p>22 GREGORY B. DIETTE, M.D.,</p> <p>23 and having been first duly sworn,</p> <p>24 was examined and testified as follows:</p> <p>25 DIRECT EXAMINATION</p>

4 (Pages 10 to 13)

Gregory B. Diette, M.D.

Page 14	Page 16
<p>1 BY MS. PARFITT:</p> <p>2 Q Good morning, Dr. Diette. How are you?</p> <p>3 A Good morning. Fine, thanks.</p> <p>4 Q Good. We will dispense with the usual</p> <p>5 comments with regard to a deposition. I</p> <p>6 understand you've had --</p> <p>7 THE VIDEOGRAPHER: Microphone.</p> <p>8 BY MS. PARFITT:</p> <p>9 Q All right. Now we're back on the mic.</p> <p>10 Dr. Diette, we'll dispense with the</p> <p>11 usual comments with regard to what a deposition is</p> <p>12 about. I understand you've probably had your</p> <p>13 deposition taken more than a hundred times. Is</p> <p>14 that fair?</p> <p>15 A I don't know if it's a hundred, but --</p> <p>16 but plenty enough that I think that I -- I</p> <p>17 understand the process.</p> <p>18 Q All right. The only one that I will ask</p> <p>19 you to pay some attention to is the fact that if</p> <p>20 you don't understand my question, please let me</p> <p>21 know. Otherwise, I'm going to assume you</p> <p>22 understand every question that I ask, and the</p> <p>23 answers that you're giving are truthful and</p> <p>24 accurate. Fair enough?</p> <p>25 A It is.</p>	<p>1 jury.</p> <p>2 A Sure. It's Gregory --</p> <p>3 MS. BROWN: Objection. There's no jury</p> <p>4 here.</p> <p>5 MS. PARFITT: There may be.</p> <p>6 MS. BROWN: Go ahead, Dr. Diette.</p> <p>7 THE WITNESS: My parents gave it to me,</p> <p>8 for what it's worth, but it's Gregory Bruce</p> <p>9 Diette.</p> <p>10 BY MS. PARFITT:</p> <p>11 Q Okay. Very good.</p> <p>12 Dr. Diette, what I'd like to do is mark</p> <p>13 as Exhibit 1 a notice of the deposition.</p> <p>14 (Diette Exhibit No. 1 was marked</p> <p>15 for identification.)</p> <p>16 BY MS. PARFITT:</p> <p>17 Q Dr. Diette, if I may, Exhibit 1 is the</p> <p>18 notice of deposition. Have you seen that document</p> <p>19 before?</p> <p>20 A Yeah, I've certainly seen -- seen</p> <p>21 something just like this.</p> <p>22 Q All right. Do you see at the back of</p> <p>23 the deposition, there is a notice that -- there is</p> <p>24 a request for you to bring certain information to</p> <p>25 your deposition? Do you see that?</p>
Page 15	Page 17
<p>1 Q All right. Now, you're sitting here</p> <p>2 today in Towson, Maryland, in a Sheraton Hotel; is</p> <p>3 that correct?</p> <p>4 A That is.</p> <p>5 Q All right. You are normally, I believe,</p> <p>6 over at Johns Hopkins University Medical Center,</p> <p>7 correct?</p> <p>8 A That's right.</p> <p>9 Q All right. Is your department aware of</p> <p>10 the fact that you're sitting over here having a</p> <p>11 deposition taken?</p> <p>12 A I don't know if anybody knows about this</p> <p>13 today, but they wouldn't be surprised, I mean, to</p> <p>14 hear it if I told them.</p> <p>15 Q All right. They know that you</p> <p>16 frequently give depositions so they would not be</p> <p>17 surprised; is that correct?</p> <p>18 MS. BROWN: Objection to form.</p> <p>19 THE WITNESS: They -- I don't know about</p> <p>20 frequently, but they know that -- that I do give</p> <p>21 depositions.</p> <p>22 BY MS. PARFITT:</p> <p>23 Q All right. Very good.</p> <p>24 Would you please introduce your formal</p> <p>25 God-given name for the ladies and gentlemen of the</p>	<p>1 A Yes.</p> <p>2 Q All right. Have you had a chance to</p> <p>3 review that?</p> <p>4 A I have.</p> <p>5 Q All right. How recently?</p> <p>6 A Last week sometime.</p> <p>7 Q All right. Was it provided to you by</p> <p>8 counsel?</p> <p>9 A I think that's the only way I could get</p> <p>10 it.</p> <p>11 Q Okay. Very good.</p> <p>12 Now, yesterday, perhaps early in the</p> <p>13 morning, I was also provided a copy of the</p> <p>14 Defendants' Response to the Plaintiffs' Document</p> <p>15 Requests Contained in the Notice of Oral and</p> <p>16 Videotaped Deposition.</p> <p>17 Let me show you what we will have marked</p> <p>18 as Exhibit No. 2.</p> <p>19 (Diette Exhibit No. 2 was marked</p> <p>20 for identification.)</p> <p>21 BY MS. PARFITT:</p> <p>22 Q Dr. Diette, let me present you with a</p> <p>23 copy of Exhibit No. 2.</p> <p>24 All right. Dr. Diette, my understanding</p> <p>25 is that this document, Exhibit No. 2, represents</p>

Gregory B. Diette, M.D.

Page 18	Page 20
<p>1 your responses to the requests that were</p> <p>2 propounded upon you to -- for documents and other</p> <p>3 materials prior to your deposition, correct?</p> <p>4 MS. BROWN: Objection to the form. It</p> <p>5 represents the lawyer's objections to the document</p> <p>6 requests you served.</p> <p>7 MS. PARFITT: Fair.</p> <p>8 THE WITNESS: I -- I think Ms. Brown's</p> <p>9 got it right.</p> <p>10 BY MS. PARFITT:</p> <p>11 Q All right. Did you -- well, let's have</p> <p>12 marked the attachment to the response to</p> <p>13 plaintiffs' document, which was prepared by your</p> <p>14 lawyers. And let's separately mark as Exhibit</p> <p>15 No. 3 the attachments, if you will.</p> <p>16 A Should I pull this apart or -- or you</p> <p>17 want to do that?</p> <p>18 Q And for purposes of the record,</p> <p>19 Exhibit 2 will represent the entire document, the</p> <p>20 response to plaintiffs' request, and No. 3 will</p> <p>21 represent just the attachments to the request,</p> <p>22 which would be material that you, Dr. Diette, were</p> <p>23 to provide.</p> <p>24 (Diette Exhibit No. 3 was marked</p> <p>25 for identification.)</p>	<p>1 much.</p> <p>2 BY MS. PARFITT:</p> <p>3 Q All right. Dr. Diette, number -- or</p> <p>4 Exhibit No. 3, the first document, Supplemental</p> <p>5 Materials Reviewed and Considered, did you prepare</p> <p>6 this Supplemental Materials Reviewed and</p> <p>7 Considered?</p> <p>8 A I contributed to it, but I didn't do the</p> <p>9 typing.</p> <p>10 Q Okay. What does that mean when you say</p> <p>11 you contributed to it?</p> <p>12 A I helped to clarify what other --</p> <p>13 because this -- this looks like it's all</p> <p>14 reports -- I just want to make sure what's here --</p> <p>15 reports, a couple of papers probably, and I -- I</p> <p>16 helped to verify that these were also things that</p> <p>17 I had -- had received and had a chance to look at.</p> <p>18 Q All right. So would it be fair to say</p> <p>19 that the 23 items listed on this were materials</p> <p>20 that somebody typed on a list and asked that you</p> <p>21 review it; is that correct?</p> <p>22 MS. BROWN: Objection to the form.</p> <p>23 Misstates his testimony.</p> <p>24 THE WITNESS: So I think, just in terms</p> <p>25 of the sequence, I mean I've gotten materials in</p>
Page 19	Page 21
<p>1 BY MS. PARFITT:</p> <p>2 Q And we'll briefly just review what's</p> <p>3 here, so we can move on to other areas.</p> <p>4 The first page of that document</p> <p>5 indicates supplemental materials reviewed and</p> <p>6 considered.</p> <p>7 MS. BROWN: Counsel, can we go off the</p> <p>8 record for a second?</p> <p>9 MS. PARFITT: Yes.</p> <p>10 THE VIDEOGRAPHER: The time is 9:03.</p> <p>11 We're going off the record.</p> <p>12 (Pause in the proceedings.)</p> <p>13 THE VIDEOGRAPHER: The time is 9:04 a.m.</p> <p>14 We're back on the record.</p> <p>15 MS. BROWN: Good morning. This is Ali</p> <p>16 Brown for J&J. We're back on the record, having</p> <p>17 taken a short break to put the cameras on both the</p> <p>18 questioner and myself, and we'll proceed, of</p> <p>19 course, with the camera on Dr. Diette. Thank you.</p> <p>20 MS. PARFITT: Thank you. And I should</p> <p>21 have asked, there's no one on the phone, is there,</p> <p>22 today?</p> <p>23 THE VIDEOGRAPHER: There is no phone</p> <p>24 present here today.</p> <p>25 MS. PARFITT: Perfect. Thank you very</p>	<p>1 this matter over a period of time, right. So they</p> <p>2 come in dribs and drabs. And a lot of this looks</p> <p>3 like some of the more recent things that came, you</p> <p>4 know, because you guys have been doing</p> <p>5 depositions, and some of the reports came in later</p> <p>6 and so forth. So it's really -- that's how I got</p> <p>7 the materials, and then this is just to make sure</p> <p>8 that I had a complete list of everything that I've</p> <p>9 gotten.</p> <p>10 BY MS. PARFITT:</p> <p>11 Q All right. And the reason I asked is</p> <p>12 because you submitted your report on</p> <p>13 February 25th, 2019. So may I assume that</p> <p>14 everything on the list, Exhibit No. 3, the first</p> <p>15 page, supplemental, represents documents you</p> <p>16 received after February 25th, 2019, correct?</p> <p>17 MS. BROWN: Objection to the form.</p> <p>18 THE WITNESS: I wouldn't assume that. I</p> <p>19 mean, so certainly some things here, right. So</p> <p>20 the expert reports that are dated 2/25, I didn't</p> <p>21 have, you know, even on the day that I submitted</p> <p>22 mine, so those came after. Something like the</p> <p>23 Barnard study, I may well have had that. I mean,</p> <p>24 my -- my goal here was to -- just to make sure</p> <p>25 that we hadn't left anything off.</p>

6 (Pages 18 to 21)

Gregory B. Diette, M.D.

Page 22	Page 24
<p>1 BY MS. PARFITT:</p> <p>2 Q All right. Is it fair to say that the</p> <p>3 items that are listed on Exhibit No. 2 -- 3 were</p> <p>4 not items that you considered for purposes of the</p> <p>5 opinions you've expressed in your report of</p> <p>6 February 25th, 2019?</p> <p>7 MS. BROWN: Objection to the form.</p> <p>8 THE WITNESS: So I -- it's very possible</p> <p>9 that the Barnard study I did consider. Trabert, I</p> <p>10 can't remember. But definitely, right, the expert</p> <p>11 reports that are dated on 2/25, I couldn't have</p> <p>12 considered. And anything that's a deposition</p> <p>13 transcript that happened after 2/25, obviously I</p> <p>14 couldn't have considered that either.</p> <p>15 BY MS. PARFITT:</p> <p>16 Q All right. Very good.</p> <p>17 The information thereafter, I believe we</p> <p>18 have -- one, two, three -- four invoices. They</p> <p>19 begin with the date of 12/14/2018, and end with a</p> <p>20 date of 3/15/19.</p> <p>21 Are there any other invoices that you</p> <p>22 would like to share with me today?</p> <p>23 A I don't have any others that I'm aware</p> <p>24 of.</p> <p>25 Q Are you preparing any invoices for your</p>	<p>1 Q All right. Let me get this straight.</p> <p>2 Your hourly rate is 485.</p> <p>3 A Well, sort of. I'll describe it if</p> <p>4 you'd like here.</p> <p>5 Q Well, I -- you can understand my</p> <p>6 confusion. If your hourly rate is 485, I want to</p> <p>7 know you're -- why I'm getting --</p> <p>8 A You don't need to be confused for very</p> <p>9 long, though.</p> <p>10 MS. BROWN: Hold on. Hold on.</p> <p>11 Counsel, you've got to let him answer</p> <p>12 the question.</p> <p>13 MS. PARFITT: Sure.</p> <p>14 MS. BROWN: He is endeavoring to set</p> <p>15 that straight.</p> <p>16 MS. PARFITT: Please.</p> <p>17 MS. BROWN: So go ahead.</p> <p>18 THE WITNESS: I think it's pretty easy.</p> <p>19 I charge \$400 an hour, and Medical Science</p> <p>20 Affiliates prepares this invoice, and part of</p> <p>21 their business model is to add an hourly rate</p> <p>22 to -- to my rate.</p> <p>23 BY MS. PARFITT:</p> <p>24 Q Okay. And I want to talk a little bit</p> <p>25 about that in a moment, but that's exactly one of</p>
Page 23	Page 25
<p>1 time post the very last invoice which is dated</p> <p>2 3/15/2019?</p> <p>3 A I will be.</p> <p>4 Q All right. How many hours have you</p> <p>5 spent since your submitting the invoice of</p> <p>6 3/15/2019?</p> <p>7 A Let's see, three -- I would estimate</p> <p>8 about -- about 20 hours or maybe 25 hours, give or</p> <p>9 take.</p> <p>10 Q All right. And what is your hourly</p> <p>11 rate?</p> <p>12 A So to clarify, so when on here it says</p> <p>13 it's 485, my -- my rate itself is actually \$400 an</p> <p>14 hour, and that's the amount that was charged.</p> <p>15 Q Okay. Now, is the amount that was</p> <p>16 charged, 400, because you worked with someone else</p> <p>17 who assists you with preparing the materials?</p> <p>18 A It's not --</p> <p>19 MS. BROWN: Objection to the form of the</p> <p>20 question.</p> <p>21 THE WITNESS: Sorry.</p> <p>22 MS. BROWN: Go ahead. You can answer.</p> <p>23 THE WITNESS: No, it's because that's</p> <p>24 how much I've asked to be paid is \$400 per hour.</p> <p>25 BY MS. PARFITT:</p>	<p>1 the issues I need some clarification on. But</p> <p>2 let's finish up the bills.</p> <p>3 A Mm-hmm.</p> <p>4 Q We have a bill for 12/14/2018 for</p> <p>5 \$17,103.75. Correct?</p> <p>6 A Correct.</p> <p>7 Q And we have a bill for 1/15/2018 for</p> <p>8 \$5,068.02, correct?</p> <p>9 A That's correct.</p> <p>10 Q We have a bill for 2/12/2019 for</p> <p>11 \$35,375. Is that correct?</p> <p>12 A It is.</p> <p>13 Q And we have a bill for \$20,973.75; is</p> <p>14 that correct?</p> <p>15 A It is.</p> <p>16 Q And then we have an additional 20, maybe</p> <p>17 25 hours that you will charge at the rate of \$400,</p> <p>18 although Medical Science Affiliates gets \$85 of</p> <p>19 that, correct?</p> <p>20 A That's correct, although I think -- I</p> <p>21 don't know if you're following -- well, that's</p> <p>22 correct. Go ahead.</p> <p>23 Q Okay. And we'll explore that in a</p> <p>24 minute.</p> <p>25 A Okay.</p>

7 (Pages 22 to 25)

Gregory B. Diette, M.D.

Page 26	Page 28
<p>1 Q Now, attached to that is -- it has an 2 exhibit on it, Plaintiffs' Exhibit No. 7, and it 3 appears to be several pages of notes. 4 Do you see that? 5 A I do. 6 Q All right. What are these notes? 7 A Well, these -- I haven't looked to see 8 for sure what's -- 9 MS. BROWN: And, Counsel, just to make 10 sure the record is clear, this was produced in 11 response per your request for his notes that were 12 marked at the Ingham deposition. So this exhibit 13 number is the marking from the Ingham deposition, 14 and these were the notes that he produced there 15 that I'm frankly sure you have access to, but in 16 the effort of cooperation, we reproduced them here 17 per your request. 18 BY MS. PARFITT: 19 Q So, Doctor -- 20 A It's -- oh, go ahead. I'm sorry. 21 Q Go ahead. You were going to tell me 22 what they are. 23 A Yeah, and I didn't know if that was 24 the -- the sufficient answer, because that's 25 literally, I guess, what they are right there.</p>	<p>1 that I just made as I was reading through 2 different articles. 3 Q Okay. Would -- 4 A No, I'm sorry. 5 Q Are you finished? 6 A No, that's just what I was going to say, 7 so these are -- it just represents just notes that 8 I was making at certain times when I was looking 9 at some of the articles. 10 Q Okay. When did you first start looking 11 at any of the articles? 12 A Sometime in -- by -- if we're talking 13 about the articles, meaning articles pertaining to 14 ovarian cancer and talcum powder, is it? 15 Q Well, it's a good question, because you 16 just said when you started looking at any of the 17 articles, are you talk- -- do these represent any 18 articles or do these represent articles of ovarian 19 cancer and talcum powder? 20 A Yeah, yeah. 21 MS. BROWN: And hold on, I think the 22 record is going to be unclear. When you say 23 "these," are you referring to what has been marked 24 as Plaintiffs' Exhibit 7 in response to your -- 25 MS. PARFITT: Correct.</p>
Page 27	Page 29
<p>1 These are -- they're an exhibit. But did you mean 2 something else, like -- 3 Q Well, now that I've had clarification by 4 your attorney, that does help a bit, but I do have 5 a couple of questions. 6 MS. MILLER: For the record, she's not 7 his attorney. She's J&J's attorney. 8 MS. PARFITT: We're going to have one 9 examiner today. So you and Ali decide who that's 10 going to be. 11 MS. BROWN: Okay. Counsel, let's keep 12 going with the questions for Dr. Diette so we 13 don't waste the doctor's time. 14 MS. PARFITT: Believe me, I don't want 15 to waste my time. So let's -- okay. I realize 16 every now and again it happens. 17 BY MS. PARFITT: 18 Q So, Dr. Diette, these are notes that you 19 prepared back at the time of the Ingham 20 deposition, correct? 21 A So not literally. Right, there are -- I 22 was asked, and I don't remember exactly what -- 23 what was on the notice, but I was asked to bring 24 any notes that I had made. So they're not 25 necessarily for the Ingham matter. They're notes</p>	<p>1 MS. BROWN: -- notice of deposition? 2 Okay. 3 THE WITNESS: So this would have been 4 sometime in 2017 that -- that I started. I don't 5 know if these notes were made in 2017, but I 6 just mean that that's the answer to when I started 7 to look at those article -- articles. 8 BY MS. PARFITT: 9 Q And we'll get to that timeline in a 10 moment. 11 Are there any additional notes that you 12 have prepared post Plaintiffs' Exhibit No. 7, 13 which I understand you presented at the Ingham 14 deposition? 15 A I don't think so. I'll give you an 16 example of something that I don't know whether you 17 consider it a note or not. 18 Q Okay. 19 A Like as I was preparing my report, I 20 would put like a -- like a little sticker on a 21 paper where I wanted to pull a quote into the -- 22 into the paper, and then I would tear that off and 23 throw it away because it wasn't, you know, useful 24 anymore. But nothing else that kind of -- that 25 looks like this.</p>

8 (Pages 26 to 29)

Gregory B. Diette, M.D.

Page 30	Page 32
<p>1 Q All right. So you would put a sticker</p> <p>2 on a paper like when I wanted to put a quote in,</p> <p>3 and then I tore it off.</p> <p>4 Are these medical records that -- or</p> <p>5 excuse me, medical articles that you were</p> <p>6 reviewing?</p> <p>7 A These are scientific articles, yeah, the</p> <p>8 ones that informed my report.</p> <p>9 Q All right. So do you have a stack of</p> <p>10 scientific and medical articles that informed your</p> <p>11 report at your office, at your home?</p> <p>12 A I've got -- I've got little piles of</p> <p>13 stuff everywhere you can look.</p> <p>14 Q Okay. Do any of them have markings on</p> <p>15 them or any stickies?</p> <p>16 A I don't think there's any stickies</p> <p>17 anymore. If they have markings, there could be</p> <p>18 some that have yellow highlights.</p> <p>19 Q All right.</p> <p>20 A But I don't think any that have like</p> <p>21 writing on them per se.</p> <p>22 Q Okay. But there might be yellow</p> <p>23 highlights on them, correct?</p> <p>24 A There sure could be, yeah. Not on all</p> <p>25 of them, but could be on some.</p>	<p>1 objections to those document requests, and</p> <p>2 Dr. Diette's testimony will be consistent with</p> <p>3 that.</p> <p>4 MS. PARFITT: My question -- are you</p> <p>5 objecting to providing me with a copy of</p> <p>6 Dr. Diette's agreement with Medical Science</p> <p>7 Affiliates?</p> <p>8 MS. BROWN: Well, we haven't even</p> <p>9 established that there is such a thing. I</p> <p>10 understand you to be getting into questions</p> <p>11 regarding Medical Sciences.</p> <p>12 MS. PARFITT: I will, yeah.</p> <p>13 MS. BROWN: I understand you've asked a</p> <p>14 number of document requests regarding Medical</p> <p>15 Sciences, and I just want to make sure that the</p> <p>16 record is clear that we have endeavored to respond</p> <p>17 to those and object accordingly.</p> <p>18 MS. PARFITT: Okay. And we're going to</p> <p>19 try and reduce the number of narrative objections</p> <p>20 if we can so we can get through this --</p> <p>21 THE WITNESS: I remember your question</p> <p>22 if you want me to answer it.</p> <p>23 BY MS. PARFITT:</p> <p>24 Q I do.</p> <p>25 I wanted to know in response to request</p>
Page 31	Page 33
<p>1 Q All right.</p> <p>2 MS. PARFITT: I'll address this with</p> <p>3 counsel later, but I would request copies of all</p> <p>4 those highlighted articles that you may have</p> <p>5 somewhere. But we can talk about that --</p> <p>6 MS. BROWN: We can talk about that off</p> <p>7 the record.</p> <p>8 THE WITNESS: Okay.</p> <p>9 BY MS. PARFITT:</p> <p>10 Q All right. So other than notations on</p> <p>11 some medical and scientific articles, there would</p> <p>12 be no additional notes like that which forms part</p> <p>13 of the part of Plaintiffs' Exhibit 7, correct?</p> <p>14 A Correct.</p> <p>15 Q All right. In the request to appear</p> <p>16 here at your deposition, there was an inquiry with</p> <p>17 regard to, I believe you called it, Medical</p> <p>18 Science Affiliates.</p> <p>19 A Correct.</p> <p>20 Q All right. Do you have a retainer</p> <p>21 agreement with Medical Science Affiliates?</p> <p>22 MS. BROWN: And I'm just going to</p> <p>23 interject here, Counsel. To the extent you've</p> <p>24 made a request for any documentation regarding</p> <p>25 Medical Science Affiliates, you have our</p>	<p>1 number 14, whether or not you have any contracts,</p> <p>2 agreements, writings conveying mutual</p> <p>3 understandings between you and Medical Science</p> <p>4 Affiliates or any entity of or related to Medical</p> <p>5 Science Affiliates for the past ten years?</p> <p>6 MS. BROWN: And, Counsel, I'm going to</p> <p>7 object to the extent that any of those requests or</p> <p>8 documentation involve work product that we have</p> <p>9 asserted privilege over, he will not be answering</p> <p>10 that question under the work-product privilege.</p> <p>11 MS. PARFITT: Okay, Counsel, you can</p> <p>12 assert work product. Got it. Is that what you're</p> <p>13 asserting right now?</p> <p>14 MS. BROWN: Yes. He's not going to</p> <p>15 answer that question. We're asserting work</p> <p>16 product.</p> <p>17 MS. PARFITT: So he is not going to</p> <p>18 answer my question with regard to any agreement or</p> <p>19 writing or contracts that he has with Medical</p> <p>20 Science Affiliates under the guidance of counsel</p> <p>21 that is objecting and refusing to have you answer</p> <p>22 that question. Is that correct -- record correct?</p> <p>23 MS. BROWN: That's correct, Counsel.</p> <p>24 MS. PARFITT: Okay.</p> <p>25 BY MS. PARFITT:</p>

Gregory B. Diette, M.D.

Page 34	Page 36
<p>1 Q And we're going to talk about Medical</p> <p>2 Science in just -- just a moment.</p> <p>3 Anything else other than the documents</p> <p>4 that I have in front of you, Exhibit 7, the</p> <p>5 invoice and your supplemental reliance, that you</p> <p>6 have brought to your deposition today?</p> <p>7 A So I didn't bring this today.</p> <p>8 Q Okay. Fair enough.</p> <p>9 A I mean I -- I didn't bring anything -- I</p> <p>10 mean I didn't bring any materials to the</p> <p>11 deposition.</p> <p>12 Q Okay.</p> <p>13 All right. Dr. Diette, what is your</p> <p>14 profession?</p> <p>15 A Well, I'm a physician, epidemiologist,</p> <p>16 researcher.</p> <p>17 Q Okay. You're actually a professor of</p> <p>18 medicine at the Department of Pulmonary and</p> <p>19 Critical Care, is that correct, at Johns Hopkins?</p> <p>20 A Literally it's the Department of</p> <p>21 Internal Medicine, and it's the Division of</p> <p>22 Pulmonary, Critical Care, and Sleep Medicine.</p> <p>23 Q Okay. Dr. Diette, do you agree that</p> <p>24 ovarian cancer ranks as the fifth cause of</p> <p>25 neoplastic death among women?</p>	<p>1 THE WITNESS: I've seen -- I've seen it</p> <p>2 ranked highly. I don't remember if it was fifth,</p> <p>3 but I've seen it ranked highly.</p> <p>4 BY MS. PARFITT:</p> <p>5 Q All right. Are you aware of the fact</p> <p>6 that ovarian cancer accounts for more deaths than</p> <p>7 any other cancer in the female reproductive</p> <p>8 system?</p> <p>9 A Ovarian cancer. Is that -- is that a</p> <p>10 statement from a -- like a document or something?</p> <p>11 Q It's a question.</p> <p>12 A It's a question that --</p> <p>13 Q Do you know whether or not ovarian</p> <p>14 cancer accounts for more deaths than any other</p> <p>15 cancer of the female reproductive system?</p> <p>16 A I know it's a highly ranked one. I</p> <p>17 wouldn't be able to say whether it's more than all</p> <p>18 others.</p> <p>19 Q All right. Do you know whether</p> <p>20 approximately 22,000 new cases of ovarian cancer</p> <p>21 identified each year and 14,000 women</p> <p>22 approximately will die in the United States alone</p> <p>23 from ovarian cancer?</p> <p>24 MS. BROWN: Objection to the form.</p> <p>25 THE WITNESS: I haven't memorized</p>
Page 35	Page 37
<p>1 A I've seen -- I've seen it listed on --</p> <p>2 you know, on lists of causes of death. I don't</p> <p>3 know what you mean by "agree with," but I mean --</p> <p>4 Q Do you have a difference of opinion as</p> <p>5 to whether or not ovarian cancer ranks fifth with</p> <p>6 regard to causes of neoplastic death among women?</p> <p>7 MS. BROWN: Objection. Asked and</p> <p>8 answered.</p> <p>9 THE WITNESS: It doesn't seem to be</p> <p>10 something that there's an opinion on. That's what</p> <p>11 I mean. I mean it's like an objective fact. I</p> <p>12 mean if there's a list that's put out by, you</p> <p>13 know, government stats, and it's number 5 on that</p> <p>14 list, that's -- that's an objective fact.</p> <p>15 BY MS. PARFITT:</p> <p>16 Q Do you object to that?</p> <p>17 MS. BROWN: Let him answer, Counsel.</p> <p>18 MS. PARFITT: I have. Thank you.</p> <p>19 Are you objecting as --</p> <p>20 BY MS. PARFITT:</p> <p>21 Q Let me ask you this, Doctor.</p> <p>22 A Okay.</p> <p>23 Q Have you seen that in any published</p> <p>24 scientific literature?</p> <p>25 MS. BROWN: Objection to the form.</p>	<p>1 anything with exact numbers like that. I mean I'm</p> <p>2 not saying it's far off from the truth, and if you</p> <p>3 have, you know, some document that supports that,</p> <p>4 I'd be glad to look at it and see if it looks</p> <p>5 right, but -- but I haven't memorized the exact</p> <p>6 number.</p> <p>7 BY MS. PARFITT:</p> <p>8 Q All right. And you know, Dr. Diette,</p> <p>9 this won't be a memory test, but I do understand</p> <p>10 that you have spent almost \$100,000 in this case</p> <p>11 alone reviewing medical and scientific articles,</p> <p>12 so all I'm simply asking is that you provide me</p> <p>13 with your best answers. Fair?</p> <p>14 MS. BROWN: I object to the --</p> <p>15 MS. PARFITT: That's all, Counsel.</p> <p>16 That's all --</p> <p>17 MS. BROWN: -- speech by counsel. He's</p> <p>18 here to answer your questions.</p> <p>19 MS. PARFITT: Counsel --</p> <p>20 MS. BROWN: That is a highly</p> <p>21 objectionable statement, Counsel, and you know it.</p> <p>22 If you have a question to ask him, he is here to</p> <p>23 answer it. We're not going to be here to have you</p> <p>24 give speeches on the record about the fees that he</p> <p>25 has charged for the work that he has done.</p>

Gregory B. Diette, M.D.

Page 38	Page 40
<p>1 MS. PARFITT: Ms. Brown, your objection,</p> <p>2 according to the CMO in the MDL case, perhaps</p> <p>3 you're doing other state depositions, is that you</p> <p>4 say, "Objection. Form."</p> <p>5 And I'll try and do my best, if you'd do</p> <p>6 the same. And I'm not admonishing you, and I hope</p> <p>7 you're not admonishing me. That's not how I roll.</p> <p>8 MS. BROWN: Well, the record is going to</p> <p>9 be very clear --</p> <p>10 MS. PARFITT: It will be.</p> <p>11 MS. BROWN: -- about the statement that</p> <p>12 you just made about the other work that I'm doing.</p> <p>13 MS. PARFITT: I said --</p> <p>14 MS. BROWN: I am well aware of the</p> <p>15 CMO --</p> <p>16 MS. PARFITT: Perfect. Okay.</p> <p>17 Counsel --</p> <p>18 MS. BROWN: -- and the deposition</p> <p>19 protocol in this case.</p> <p>20 MS. PARFITT: -- that's fine.</p> <p>21 MS. BROWN: And I --</p> <p>22 MS. PARFITT: Counsel --</p> <p>23 MS. BROWN: -- expect that you will</p> <p>24 abide by it --</p> <p>25 MS. PARFITT: -- let me ask questions.</p>	<p>1 thinking about your question before, I just wanted</p> <p>2 to clarify that I -- because when you said that I</p> <p>3 billed \$100,000, I think what you might be doing</p> <p>4 is adding up all of those MSA invoices, which that</p> <p>5 doesn't all go to me. I mean there's a way to</p> <p>6 figure out how much that I've billed, but -- but</p> <p>7 you wouldn't be correct if you're saying that</p> <p>8 those four invoices represent the amount that I've</p> <p>9 charged.</p> <p>10 Q Okay. And we'll talk about that, but I</p> <p>11 appreciate the clarification.</p> <p>12 So, the other question is, do you have</p> <p>13 an understanding that most ovarian cancer cases</p> <p>14 are detected and diagnosed at a late stage and</p> <p>15 there are limited prospects for cure?</p> <p>16 MS. BROWN: Same objection.</p> <p>17 THE WITNESS: I have that general</p> <p>18 understanding.</p> <p>19 BY MS. PARFITT:</p> <p>20 Q Okay. Do you have any knowledge as to</p> <p>21 what the mortality and morbidity of ovarian cancer</p> <p>22 is?</p> <p>23 A Well, the morbidity is not a number,</p> <p>24 right. I mean you're talking about what are the</p> <p>25 consequences?</p>
Page 39	Page 41
<p>1 MS. BROWN: -- and not interrupt me.</p> <p>2 Thank you.</p> <p>3 MS. PARFITT: I am not going to, but I</p> <p>4 would ask the same courtesy. And, listen, we have</p> <p>5 a long day to go, and it will be longer --</p> <p>6 MS. BROWN: Just ask the doctor a</p> <p>7 question and move on.</p> <p>8 MS. PARFITT: -- if we go back and</p> <p>9 forth. "Objection, form" is the appropriate way,</p> <p>10 or we will have to call the judge.</p> <p>11 MS. BROWN: Happy to do it.</p> <p>12 MS. PARFITT: Very good. So will I.</p> <p>13 BY MS. PARFITT:</p> <p>14 Q All right. Dr. Diette, do you have an</p> <p>15 understanding from your review of the scientific</p> <p>16 and medical literature that ovarian cancer cases</p> <p>17 are detected and diagnosed at a late stage and</p> <p>18 there are limited prospects for cure?</p> <p>19 MS. BROWN: Objection to the form of the</p> <p>20 question.</p> <p>21 THE WITNESS: I didn't listen to what</p> <p>22 you said because --</p> <p>23 BY MS. PARFITT:</p> <p>24 Q Sure.</p> <p>25 A But just for the reason that I'm still</p>	<p>1 Q You're right.</p> <p>2 A And then the mortality would be</p> <p>3 something that's an objective fact that there's a</p> <p>4 percentage of people with the disease that die.</p> <p>5 Q Right.</p> <p>6 A I don't know the number. I didn't</p> <p>7 memorize that. If it's important, we can look it</p> <p>8 up, but it's a high -- it's a high proportion that</p> <p>9 die from it.</p> <p>10 Q Fair. Do you know what the latency is</p> <p>11 for ovarian cancer?</p> <p>12 A Between what and what?</p> <p>13 Q The latency period between -- let's take</p> <p>14 some examples -- asbestos and ovarian cancer.</p> <p>15 MS. BROWN: Objection to the form of the</p> <p>16 question.</p> <p>17 You can answer if you understand.</p> <p>18 THE WITNESS: So the -- that's a tricky</p> <p>19 issue, I think in a way, because I'm not sure that</p> <p>20 it's been fully established that asbestos causes</p> <p>21 ovarian cancer. I mean I'm aware of what the IARC</p> <p>22 has put out on it, but I'm not sure that that's a</p> <p>23 fact. But I don't recall seeing in there where</p> <p>24 the latency, if it was even true, whether that</p> <p>25 was -- whether that was established.</p>

11 (Pages 38 to 41)

Gregory B. Diette, M.D.

Page 42	Page 44
<p>1 BY MS. PARFITT:</p> <p>2 Q All right. Have you in the course of --</p> <p>3 strike that.</p> <p>4 All right. From a review of the</p> <p>5 materials you reviewed attached to your expert</p> <p>6 report, Doctor, I see that you reviewed the Purdie</p> <p>7 case --</p> <p>8 MS. BROWN: Counsel -- Counsel, is there</p> <p>9 a page you want to point him to so we can follow</p> <p>10 along?</p> <p>11 MS. PARFITT: I'm still asking the</p> <p>12 question, Counsel.</p> <p>13 BY MS. PARFITT:</p> <p>14 Q Dr. Diette, attached to your report is a</p> <p>15 materials reviewed. And on page 7, it lists that</p> <p>16 you have read the Purdie case, which is a 1995</p> <p>17 case study -- excuse me, not case study, but a</p> <p>18 scientific article.</p> <p>19 MS. BROWN: Objection to the form.</p> <p>20 Take your time to get to that page,</p> <p>21 Doctor.</p> <p>22 THE WITNESS: It's 7 in my report?</p> <p>23 BY MS. PARFITT:</p> <p>24 Q It is on page 7 of your report.</p> <p>25 MS. BROWN: And, Counsel, I think we</p>	<p>1 Q Okay. All right. And we're going to</p> <p>2 talk about that in conjunction with -- just hold</p> <p>3 tight. I'm going to set that aside, and let me</p> <p>4 ask you this --</p> <p>5 A Can I ask just real quick?</p> <p>6 Q Sure.</p> <p>7 A There's like a cold breeze blowing down</p> <p>8 here, and I know we will regret making it warmer</p> <p>9 in here at some point.</p> <p>10 Q Sure.</p> <p>11 MS. PARFITT: Well, let's take a moment</p> <p>12 and let's see if we can --</p> <p>13 MS. BROWN: Why don't we go off the</p> <p>14 record for one second.</p> <p>15 THE VIDEOGRAPHER: The time is 9:25 a.m.</p> <p>16 We're going off the record.</p> <p>17 (Pause in the proceedings.)</p> <p>18 THE VIDEOGRAPHER: The time is 9:27 a.m.</p> <p>19 and we are back on the record.</p> <p>20 (Diette Exhibit No. 4 was marked</p> <p>21 for identification.)</p> <p>22 MS. PARFITT: Ready?</p> <p>23 THE VIDEOGRAPHER: Oh, yeah, we're on.</p> <p>24 MS. PARFITT: Okay. Thank you.</p> <p>25 BY MS. PARFITT:</p>
Page 43	Page 45
<p>1 have a disconnect here. Are you referring to the</p> <p>2 7 of the reliance list?</p> <p>3 MS. PARFITT: I am. I'm sorry about</p> <p>4 that.</p> <p>5 THE WITNESS: Oh. Is it 7 of the -- the</p> <p>6 exhibit you gave me or is it part of what's my</p> <p>7 reliance list that's attached to my report?</p> <p>8 BY MS. PARFITT:</p> <p>9 Q What I have is your reliance list, and</p> <p>10 it's page 7 of your reliance list.</p> <p>11 A I got you.</p> <p>12 MS. BROWN: Got that. Okay.</p> <p>13 BY MS. PARFITT:</p> <p>14 Q And I believe you have three Purdie --</p> <p>15 excuse me, two Purdie cites, one 2003 and one</p> <p>16 1995. Correct?</p> <p>17 A That's correct.</p> <p>18 Q Okay. Did you indeed review the Purdie</p> <p>19 article for purposes of your testimony here today?</p> <p>20 MS. BROWN: Objection to the form.</p> <p>21 THE WITNESS: I don't think I reviewed</p> <p>22 it for the purpose of my testimony, but I -- I</p> <p>23 included it because it's something I reviewed at</p> <p>24 some point prior to preparing the report.</p> <p>25 BY MS. PARFITT:</p>	<p>1 Q Dr. Diette, let me show you what's been</p> <p>2 marked as Plaintiffs' Exhibit No. 4 to the Diette</p> <p>3 deposition, and I'll represent to you -- sorry --</p> <p>4 I'll represent to you that this is the --</p> <p>5 MS. BROWN: Thank you.</p> <p>6 BY MS. PARFITT:</p> <p>7 Q -- an article by Dr. Purdie entitled</p> <p>8 "Ovulation and Risk of Epithelial Ovarian Cancer"</p> <p>9 published in the International Journal of Cancer</p> <p>10 in 2003. Do you see that?</p> <p>11 A I do.</p> <p>12 Q All right. If I can direct your</p> <p>13 attention to page 231 of that article.</p> <p>14 MS. PARFITT: Let's put it on the ELMO.</p> <p>15 BY MS. PARFITT:</p> <p>16 Q Okay. And, Dr. Diette, I'll put it up</p> <p>17 on the overhead as well. About halfway down --</p> <p>18 there you go -- left-hand column, Dr. Purdie and</p> <p>19 authors state: "Thus, the latency period of more</p> <p>20 advanced malignant epithelial ovarian cancer could</p> <p>21 be estimated to be approximately 30 to 40 years."</p> <p>22 Did I read that correctly?</p> <p>23 A You read it fine.</p> <p>24 Q All right. Do you agree or disagree</p> <p>25 that the latency period of more advanced malignant</p>

12 (Pages 42 to 45)

Gregory B. Diette, M.D.

Page 46	Page 48
<p>1 epithelial ovarian cancer can be estimated to be</p> <p>2 approximately 30 to 40 years?</p> <p>3 A Well, I think, you know -- so there's no</p> <p>4 way for me to know for sure, right, but could</p> <p>5 be -- it seems like a pretty safe statement</p> <p>6 because it could be more, it could be less.</p> <p>7 It's also an incomplete sentence, right,</p> <p>8 in the sense that when you talk about the latency,</p> <p>9 you talk about the latency between a particular</p> <p>10 kind of exposure. I mean, in this context, right,</p> <p>11 there may have other -- there may be other ways</p> <p>12 people use that word, but in this context it's the</p> <p>13 time from the exposure to the development of the</p> <p>14 disease. So there's no exposure mentioned in that</p> <p>15 sentence, so it's a little -- a little loose, you</p> <p>16 know.</p> <p>17 MS. PARFITT: All right. Move to strike</p> <p>18 that last part of your statement.</p> <p>19 BY MS. PARFITT:</p> <p>20 Q Okay. Dr. Diette, do you agree that</p> <p>21 it's imperative to develop public health programs</p> <p>22 that either reduce the incidence or detect ovarian</p> <p>23 cancer at an earlier stage?</p> <p>24 A It's an agreeable statement.</p> <p>25 Q Okay. In developing public health</p>	<p>1 BY MS. PARFITT:</p> <p>2 Q Sure. And, you know, that might be --</p> <p>3 that might be fair. So let me go for a third try.</p> <p>4 Okay?</p> <p>5 A Okay.</p> <p>6 Q Do you develop public health programs</p> <p>7 for Johns Hopkins?</p> <p>8 A I'm trying to think -- I would say</p> <p>9 generally, no. I mean --</p> <p>10 Q It's not part of your role.</p> <p>11 MS. BROWN: Well, let him finish. I'm</p> <p>12 sorry.</p> <p>13 THE WITNESS: But I don't know -- I</p> <p>14 mean, I don't know what -- I mean that's a pretty</p> <p>15 broad topic, which is what's a public health</p> <p>16 program. So I'm just thinking like, for example,</p> <p>17 you know, I've done work with asthma in -- in the</p> <p>18 inner city nearby.</p> <p>19 BY MS. PARFITT:</p> <p>20 Q Correct.</p> <p>21 A And we certainly have a program, you</p> <p>22 know, that deals with -- with that. I wouldn't</p> <p>23 say I've developed it as a public health program</p> <p>24 per se but as a -- as a research program. But,</p> <p>25 you know, where public health starts and stops,</p>
Page 47	Page 49
<p>1 programs, does -- in order to set up preventive</p> <p>2 programs, detection programs, does that include</p> <p>3 getting information about whatever the putative</p> <p>4 exposure may be to individuals who may be</p> <p>5 susceptible to them?</p> <p>6 MS. BROWN: Objection to the form of the</p> <p>7 question.</p> <p>8 MS. PARFITT: Let me strike that</p> <p>9 question completely. It was a lousy question.</p> <p>10 All right.</p> <p>11 THE WITNESS: It was --</p> <p>12 MS. PARFITT: And I'm going to agree</p> <p>13 with counsel on that. How about that?</p> <p>14 THE WITNESS: It was below average. It</p> <p>15 wasn't lousy.</p> <p>16 BY MS. PARFITT:</p> <p>17 Q Sure. Okay.</p> <p>18 When one develops a public health</p> <p>19 program in order to alert individuals about a</p> <p>20 public health issue, what is the manner, let's</p> <p>21 say, in your department to do that?</p> <p>22 MS. BROWN: Objection to the form of the</p> <p>23 question.</p> <p>24 THE WITNESS: I'm not sure what we're</p> <p>25 talking about. I mean --</p>	<p>1 I'm not exactly sure.</p> <p>2 Q Fair enough.</p> <p>3 All right. Talcum powder products are</p> <p>4 widely available, correct?</p> <p>5 MS. BROWN: Objection to the form of the</p> <p>6 question.</p> <p>7 THE WITNESS: You know, they -- I</p> <p>8 guess -- so anyway, I'm an epidemiologist, so when</p> <p>9 somebody says something like that, like when you</p> <p>10 say it, like I'm thinking like to whom or for whom</p> <p>11 or where or when or something. I mean there's</p> <p>12 sort of like a time and place and something else</p> <p>13 more to that. I think it's a common product, but</p> <p>14 I don't -- I don't know what it means to be widely</p> <p>15 available.</p> <p>16 BY MS. PARFITT:</p> <p>17 Q All right. Did you ever ask Johnson &</p> <p>18 Johnson or their attorneys a question with regard</p> <p>19 to how many bottles of Johnson & Johnson's Baby</p> <p>20 Powder they distribute each year in America?</p> <p>21 MS. BROWN: Objection to the form of the</p> <p>22 question.</p> <p>23 THE WITNESS: I have not asked that.</p> <p>24 BY MS. PARFITT:</p> <p>25 Q Okay. Similarly, have you ever asked</p>

Gregory B. Diette, M.D.

Page 50	Page 52
<p>1 Johnson & Johnson how many bottles of their Shower 2 to Shower they distributed? 3 A No. 4 MS. BROWN: Same objection. 5 BY MS. PARFITT: 6 Q All right. Have you ever purchased 7 talcum powder products? 8 A I -- I don't do the shopping. You know, 9 and so it -- like, I don't -- I don't buy anything 10 at the store. 11 Q Okay. Fair enough. 12 Are you aware of the fact that Johnson & 13 Johnson continues to sell their talcum powder 14 products? 15 A I wasn't aware that they weren't. I 16 mean, I don't know where I would get that from, 17 but as best as I can tell. 18 Q All right. Have you ever looked at the 19 back of a Johnson & Johnson's Baby Powder product 20 to see what it says about its usage -- 21 MS. BROWN: Objection. 22 BY MS. PARFITT: 23 Q -- and direction? 24 MS. BROWN: Excuse me. Objection to the 25 form of the question.</p>	<p>1 BY MS. PARFITT: 2 Q Okay. Let me show you what I'll have 3 marked as Exhibit -- 4 MS. PARFITT: Where are we? 5 MR. ROSEN: Five. 6 BY MS. PARFITT: 7 Q -- 5. And I'll represent to you, 8 Dr. Diette, that this is a bottle of Johnson's 9 Baby Powder, and we'll have it marked as Exhibit 10 No. 5. 11 (Diette Exhibit No. 5 was marked 12 for identification.) 13 BY MS. PARFITT: 14 Q Now, my understanding is that you are 15 trained, skilled, and have expertise in pulmonary 16 medicine, correct? 17 A Among other things. 18 Q And I didn't mean to limit your 19 expertise. Okay. 20 If you will, let me show -- pass to you 21 the Exhibit No. 5, and ask that you turn it to the 22 back. Look at the bottle. 23 MS. BROWN: Counsel, before he does 24 that, will you put -- represent on the record 25 where this bottle that you've marked as Exhibit 5</p>
Page 51	Page 53
<p>1 THE WITNESS: It's possible that I have 2 years ago, but not -- not recently. 3 BY MS. PARFITT: 4 Q Nothing recent. 5 How about since you were retained by 6 Johnson & Johnson as an expert, have you ever 7 looked at a bottle of Johnson & Johnson's Baby 8 Powder or Shower to Shower? 9 MS. BROWN: Same objection. 10 THE WITNESS: No. I've seen pictures, 11 you know, in different settings, but I haven't -- 12 I haven't seen a bottle of it or looked at it. 13 BY MS. PARFITT: 14 Q Okay. Do you have an understanding as 15 to whether or not Johnson & Johnson's Baby Powder 16 or the Shower to Shower contains a warning on its 17 product against use in the genital area to avoid 18 ovarian cancer? 19 MS. BROWN: Objection to the form. 20 THE WITNESS: I don't know whether they 21 do or don't. But I'm also not, you know, skilled 22 in warnings. So I wouldn't -- I mean, I -- even 23 if it said something, I wouldn't necessarily be 24 the person to tell you whether that's a warning or 25 not.</p>	<p>1 came from and when it was purchased and by whom? 2 MS. PARFITT: Counsel, I'm asking the 3 questions. I just represent that it is a bottle 4 of Johnson & Johnson's Baby Powder purchased from 5 a store. 6 MS. MILLER: Michelle, I'm trying 7 really, really hard not to say a word today. 8 MS. PARFITT: Sure. 9 MS. MILLER: I know that I'll annoy 10 you -- 11 MS. PARFITT: Oh, no, you're not. 12 MS. MILLER: -- but it's not Johnson & 13 Johnson's Baby Powder. It's Johnson's Baby 14 Powder, and you keep saying it wrong. 15 MS. PARFITT: That's fine. That's fine. 16 MS. MILLER: And I think for the record, 17 it's important. It's a product by JJCI, as you 18 know. 19 MS. PARFITT: That's fine. 20 MS. MILLER: So we just need 21 Johnson's -- 22 MS. PARFITT: Okay. And why don't we -- 23 whenever I -- since I'm sure I won't remember all 24 that, why don't we just reflect for the record 25 that when I say Johnson & Johnson's Baby Powder,</p>

14 (Pages 50 to 53)

Gregory B. Diette, M.D.

Page 54	Page 56
<p>1 that it's Johnson's Baby Powder. Okay?</p> <p>2 MS. BROWN: And just to get my -- my</p> <p>3 objection on the record to what you marked as</p> <p>4 Exhibit 5, we have no representation of when this</p> <p>5 was bought, by whom it was bought.</p> <p>6 With that, Dr. Diette, here is</p> <p>7 Exhibit 5.</p> <p>8 MS. PARFITT: Thank you.</p> <p>9 BY MS. PARFITT:</p> <p>10 Q All right, Dr. Diette, look at the back</p> <p>11 of that. Do you see that there's a little picture</p> <p>12 that looks like a little baby with an X on it?</p> <p>13 A I do.</p> <p>14 MS. BROWN: Objection to the form.</p> <p>15 BY MS. PARFITT:</p> <p>16 Q Okay. Okay. What does that say on the</p> <p>17 back of the product?</p> <p>18 A It says: "Warning: Keep powder away</p> <p>19 from child's face to avoid inhalation, which can</p> <p>20 cause breathing problems. Avoid contact with the</p> <p>21 eyes. For external use only."</p> <p>22 Q Okay. And at the bottom of that</p> <p>23 product, does it happen to say what's contained in</p> <p>24 it?</p> <p>25 MS. BROWN: Objection to the form of the</p>	<p>1 expert work for them?</p> <p>2 MS. BROWN: Objection to the form.</p> <p>3 THE WITNESS: I believe so, yeah.</p> <p>4 BY MS. PARFITT:</p> <p>5 Q Okay. Had you ever worked for Johnson &</p> <p>6 Johnson or any of their entities prior to 2017 in</p> <p>7 any type of litigation?</p> <p>8 MS. BROWN: Same objection.</p> <p>9 THE WITNESS: I -- I don't think so. I</p> <p>10 would say almost certainly no.</p> <p>11 BY MS. PARFITT:</p> <p>12 Q Okay. Since your retention in 2017, did</p> <p>13 Johnson & Johnson, their medical department, their</p> <p>14 regulatory department, science department, ever</p> <p>15 ask that you take a look at the back of the</p> <p>16 product, Johnson's Baby Powder, for purposes of</p> <p>17 giving an opinion as to what scientific and</p> <p>18 medical information should be on that product?</p> <p>19 MS. BROWN: Objection to the form of the</p> <p>20 question.</p> <p>21 THE WITNESS: I would be the wrong kind</p> <p>22 of expert for that. I mean I'm not a warnings</p> <p>23 expert, so it wouldn't -- wouldn't make any sense</p> <p>24 for anybody to ask me that question.</p> <p>25 BY MS. PARFITT:</p>
Page 55	Page 57
<p>1 question.</p> <p>2 THE WITNESS: It has a line called</p> <p>3 "Ingredients," which says "Talc, fragrance."</p> <p>4 BY MS. PARFITT:</p> <p>5 Q Okay. Dr. Diette, you've been retained</p> <p>6 by Johnson & Johnson since when, for purposes of</p> <p>7 the ovarian cancer cases?</p> <p>8 MS. BROWN: Objection. Form. Do you</p> <p>9 mean the Ingham case or do you mean the MDL?</p> <p>10 BY MS. PARFITT:</p> <p>11 Q Well, let me clarify.</p> <p>12 When were you first -- it's a fair</p> <p>13 question -- when were you first retained by</p> <p>14 Johnson & Johnson to represent them in either</p> <p>15 mesothelioma cases or ovarian cancer cases?</p> <p>16 MS. BROWN: Objection to the form. He</p> <p>17 is an expert witness on behalf of Johnson &</p> <p>18 Johnson. He is not here representing anyone.</p> <p>19 THE WITNESS: That honestly sounds like</p> <p>20 Ms. Brown's job, I mean, but -- but I guess to try</p> <p>21 to answer your question, the -- I was first asked</p> <p>22 to review the epidemiology in 2017.</p> <p>23 BY MS. PARFITT:</p> <p>24 Q Okay. And was that the first time that</p> <p>25 Johnson & Johnson had asked you to provide any</p>	<p>1 Q I'm not asking you about the adequacy of</p> <p>2 the warning. I'm asking you about your expertise</p> <p>3 as a pulmonary medicine expert with regard to</p> <p>4 inhalation issues as contained on the back of that</p> <p>5 product.</p> <p>6 A It still wouldn't make any sense. I</p> <p>7 wouldn't be the person to ask that to.</p> <p>8 Q Dr. Diette, whether or not it makes</p> <p>9 sense to you or not, my question is simply this:</p> <p>10 Yes or no, has Johnson & Johnson asked your</p> <p>11 opinion at any point in time with regard to what</p> <p>12 kind of scientific and medical information should</p> <p>13 be on the back of their powder?</p> <p>14 MS. BROWN: Objection. Answered three</p> <p>15 times.</p> <p>16 THE WITNESS: They and everybody else in</p> <p>17 the world has not asked me to do anything like</p> <p>18 that ever.</p> <p>19 BY MS. PARFITT:</p> <p>20 Q Okay. And they, Johnson & Johnson, has</p> <p>21 never asked you to -- your opinion with regard to</p> <p>22 the inhalation warning; is that correct?</p> <p>23 MS. BROWN: Objection. Counsel, we've</p> <p>24 been through this like six times.</p> <p>25 THE WITNESS: I think it's the same</p>

15 (Pages 54 to 57)

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 58</p> <p>1 warning we're talking about, right?</p> <p>2 BY MS. PARFITT:</p> <p>3 Q The one that's on the back, yeah.</p> <p>4 A So it's still -- still the same.</p> <p>5 Q Okay. And just for the record, we're</p> <p>6 going to put on the ELMO -- thank you. Just go</p> <p>7 ahead and see if we can get that on there. Okay.</p> <p>8 (Counsel conferring.)</p> <p>9 BY MS. PARFITT:</p> <p>10 Q And again, for clarity of the record,</p> <p>11 what we've been talking about is on -- the child</p> <p>12 with the X over the nose and mouth and the warning</p> <p>13 that is to the far right, correct?</p> <p>14 MS. BROWN: Objection to the form.</p> <p>15 THE WITNESS: I was with you until you</p> <p>16 said "to the far right." I don't know --</p> <p>17 BY MS. PARFITT:</p> <p>18 Q To the right of the baby.</p> <p>19 A Oh, I see. I'm sorry.</p> <p>20 Q Yeah, no problem.</p> <p>21 A Yeah. No, that's --</p> <p>22 Q That's what we're talking about.</p> <p>23 A It's to the right of the baby, yeah.</p> <p>24 Q Okay. Very good. All right.</p> <p>25 Dr. Diette, as a scientist and a</p>	<p style="text-align: right;">Page 60</p> <p>1 you have who have a different opinion with regard</p> <p>2 to the causality of talcum powder products and</p> <p>3 ovarian cancer?</p> <p>4 MS. BROWN: Objection to the form.</p> <p>5 THE WITNESS: Well, I've seen like, for</p> <p>6 example, the expert reports that are -- that are</p> <p>7 part of this matter and some of the deposition</p> <p>8 transcripts. So -- so, yes, I mean I've seen what</p> <p>9 they've said.</p> <p>10 BY MS. PARFITT:</p> <p>11 Q Okay. And from your review of those</p> <p>12 expert reports, do you understand that many of</p> <p>13 those scientists and epidemiologists are</p> <p>14 individuals who treat women who have been</p> <p>15 diagnosed for ovarian cancer? Do you understand</p> <p>16 that?</p> <p>17 MS. BROWN: Objection. Lacks</p> <p>18 foundation, calls for speculation.</p> <p>19 THE WITNESS: So I saw that there were</p> <p>20 some GYN oncologists involved. I don't remember</p> <p>21 the count of them, but I saw there were GYN</p> <p>22 oncologists, both on the defense and the</p> <p>23 plaintiffs' side.</p> <p>24 BY MS. PARFITT:</p> <p>25 Q Okay. And the GYN oncologists would be</p>
<p style="text-align: right;">Page 59</p> <p>1 clinician, do you have a belief or opinion that</p> <p>2 women should be informed of even a potential risk</p> <p>3 of using talcum powder products on their genital</p> <p>4 area?</p> <p>5 MS. BROWN: Objection.</p> <p>6 THE WITNESS: Not based on what I've</p> <p>7 reviewed.</p> <p>8 BY MS. PARFITT:</p> <p>9 Q Okay. Is it your opinion that there is</p> <p>10 no risk of ovarian cancer from the long-term use</p> <p>11 of talcum powder products?</p> <p>12 MS. BROWN: Objection. Form.</p> <p>13 THE WITNESS: I -- I don't see evidence</p> <p>14 that there's a -- so I'm an epidemiologist, so the</p> <p>15 way I talk about things might be a little</p> <p>16 different than the way you're asking it. But</p> <p>17 there's not sufficient evidence to say that it's a</p> <p>18 cause of ovarian cancer.</p> <p>19 BY MS. PARFITT:</p> <p>20 Q Okay. And we'll talk about that in a</p> <p>21 little bit.</p> <p>22 Do you have an understanding as to</p> <p>23 whether there are other scientists and</p> <p>24 epidemiologists who have reviewed the same</p> <p>25 scientific and epidemiological information that</p>	<p style="text-align: right;">Page 61</p> <p>1 the practice of medicine that treats women for</p> <p>2 reproductive diseases and cancers like ovarian</p> <p>3 cancer, correct?</p> <p>4 MS. BROWN: Objection.</p> <p>5 THE WITNESS: They -- they would be the</p> <p>6 ones that provide treatment for the GYN cancers.</p> <p>7 BY MS. PARFITT:</p> <p>8 Q Okay. You're a pulmonologist, correct?</p> <p>9 A I am.</p> <p>10 Q All right.</p> <p>11 A And again, among other things.</p> <p>12 Q Understood.</p> <p>13 MS. BROWN: Let him finish, Counsel, he</p> <p>14 wasn't done.</p> <p>15 BY MS. PARFITT:</p> <p>16 Q My -- it's a simple question, are you a</p> <p>17 pulmonologist?</p> <p>18 MS. BROWN: Wait, but he was still</p> <p>19 answering. You cut him off. Let him finish.</p> <p>20 MS. PARFITT: Doc -- I withdraw that</p> <p>21 question.</p> <p>22 BY MS. PARFITT:</p> <p>23 Q Are you a pulmonologist?</p> <p>24 A I am a pulmonologist.</p> <p>25 Q All right. As a pulmonologist, do you</p>

Gregory B. Diette, M.D.

Page 62	Page 64
<p>1 treat and care for women -- treat and care and</p> <p>2 provide gynecological and oncological care to</p> <p>3 women who have been diagnosed with ovarian cancer?</p> <p>4 MS. BROWN: Objection to the form.</p> <p>5 THE WITNESS: Mostly, no, although</p> <p>6 I'll just -- there was a lot in your question,</p> <p>7 right, so that --</p> <p>8 BY MS. PARFITT:</p> <p>9 Q You want me to break it down?</p> <p>10 MS. BROWN: Let him finish first, and</p> <p>11 then you can follow up. He has to be allowed to</p> <p>12 answer your question.</p> <p>13 MS. PARFITT: Oh, absolutely, but if</p> <p>14 it's unclear -- that was one of the --</p> <p>15 THE WITNESS: I didn't say it was</p> <p>16 unclear. I just said it -- it's complicated, so</p> <p>17 there's more than -- it's not just a simple</p> <p>18 answer.</p> <p>19 MS. PARFITT: Let me withdraw the</p> <p>20 question.</p> <p>21 MS. BROWN: Wait, Counsel, he's not</p> <p>22 done.</p> <p>23 Dr. Diette, you finish your answer, and</p> <p>24 then counsel, of course, will follow up.</p> <p>25 BY MS. PARFITT:</p>	<p>1 that.</p> <p>2 BY MS. PARFITT:</p> <p>3 Q Okay. What is your understanding of the</p> <p>4 testing that's been performed by Johnson & Johnson</p> <p>5 on their talcum powder products?</p> <p>6 MS. BROWN: Objection. That's overly</p> <p>7 broad.</p> <p>8 THE WITNESS: Well, like the type --</p> <p>9 MS. BROWN: You mean internal, external,</p> <p>10 third party, FDA?</p> <p>11 BY MS. PARFITT:</p> <p>12 Q Do you understand the question?</p> <p>13 A I was actually going to say something</p> <p>14 similar to what Ms. Brown said but less</p> <p>15 sophisticated.</p> <p>16 I mean what I meant was, were you asking</p> <p>17 about like the kinds of tests that were done or --</p> <p>18 or things of that sort? I just -- I just know,</p> <p>19 generally speaking, that there has been testing</p> <p>20 done.</p> <p>21 Q Sure. Let me make it very simple.</p> <p>22 Are you aware of studies -- strike that.</p> <p>23 Have you seen studies done by Johnson &</p> <p>24 Johnson that tested and evaluated their talcum</p> <p>25 powder products for the presence of asbestos?</p>
Page 63	Page 65
<p>1 Q Okay. Go ahead.</p> <p>2 A Thank you.</p> <p>3 Q Sure.</p> <p>4 A So, you know, I wouldn't be the person</p> <p>5 who prescribes chemotherapy or provides the</p> <p>6 surgery. Part of my work is as an intensive care</p> <p>7 doc in the oncology center, and so I'll see people</p> <p>8 with every kind of cancer possible and provide</p> <p>9 some of the care to them.</p> <p>10 I see people in my clinic that have, you</p> <p>11 know, pulmonary consequences of some of their</p> <p>12 treatment for ovarian cancer. And so it's -- it's</p> <p>13 not a straightforward yes or no that I do or don't</p> <p>14 participate, but I don't do the -- the GYN onc</p> <p>15 part of that care.</p> <p>16 Q All right. Have you in your practice of</p> <p>17 pulmonary medicine ever diagnosed a woman with</p> <p>18 ovarian cancer?</p> <p>19 A I can't remember ever doing that.</p> <p>20 Q All right. Now, Dr. Diette, are you</p> <p>21 aware of whether or not -- strike that.</p> <p>22 Are you aware that Johnson & Johnson has</p> <p>23 tested their talcum powder products?</p> <p>24 MS. BROWN: Objection to the form.</p> <p>25 THE WITNESS: I have some awareness of</p>	<p>1 MS. BROWN: Same objection.</p> <p>2 THE WITNESS: I don't think I've seen</p> <p>3 anything from Johnson & Johnson, per se.</p> <p>4 Is that what -- is that what you're</p> <p>5 referring to?</p> <p>6 BY MS. PARFITT:</p> <p>7 Q That is, yes.</p> <p>8 A Okay. Then not -- not that I'm aware</p> <p>9 of.</p> <p>10 Q All right. I saw where you looked at</p> <p>11 the depositions of Drs. Longo and Rigler.</p> <p>12 MS. BROWN: Objection to the form.</p> <p>13 THE WITNESS: Is that in a different</p> <p>14 case?</p> <p>15 BY MS. PARFITT:</p> <p>16 Q Good question. You have their</p> <p>17 depositions listed as part of the materials</p> <p>18 reviewed and relied upon. Have you read those?</p> <p>19 MS. BROWN: Objection.</p> <p>20 If you want to refresh yourself on your</p> <p>21 reliance list, I'm sure counsel will point you to</p> <p>22 the page.</p> <p>23 MS. PARFITT: Absolutely.</p> <p>24 BY MS. PARFITT:</p> <p>25 Q Let me direct you to -- just bear with</p>

17 (Pages 62 to 65)

Gregory B. Diette, M.D.

Page 66	Page 68
<p>1 me one second. I apologize here.</p> <p>2 Okay. It's -- your reference materials</p> <p>3 reviewed and considered start on -- or in</p> <p>4 Appendix B of your report.</p> <p>5 Do you see that?</p> <p>6 A I don't see Longo and Rigler.</p> <p>7 Q Okay. At the very top, it has</p> <p>8 "Materials Reviewed and Considered by Gregory</p> <p>9 Diette," and the second item under "Expert</p> <p>10 References" says "Expert report of William Longo</p> <p>11 and Mark Rigler."</p> <p>12 Do you see that?</p> <p>13 A Oh, I do, yeah. So I see Longo, and I'm</p> <p>14 just --</p> <p>15 Q Do you see Rigler? He's right after</p> <p>16 that. It says William --</p> <p>17 A Oh, got you.</p> <p>18 MS. BROWN: Counsel, these are reports.</p> <p>19 I thought your question was about a deposition.</p> <p>20 MS. PARFITT: That's a -- that's a fair</p> <p>21 objection.</p> <p>22 BY MS. PARFITT:</p> <p>23 Q Have you read the expert report of</p> <p>24 William Longo and Mark Rigler?</p> <p>25 A So, because I see there's a date on it</p>	<p>1 Q But my question --</p> <p>2 MS. PARFITT: And noted.</p> <p>3 BY MS. PARFITT:</p> <p>4 Q My question to you is, sitting here</p> <p>5 today, what I need to know -- and if it's no,</p> <p>6 that's a fine answer. If it's yes, that's a fine</p> <p>7 answer.</p> <p>8 Have you read the expert report of</p> <p>9 Drs. Longo and Rigler dated November 14, 2018?</p> <p>10 If you did, I'm not -- I'm not --</p> <p>11 MS. BROWN: Objection to the form. I</p> <p>12 think he answered that.</p> <p>13 Counsel, I think what you're really</p> <p>14 after is, is he relying on that to form his</p> <p>15 opinion.</p> <p>16 MS. PARFITT: Actually, I'm not. That's</p> <p>17 a good question, but I'm not asking that.</p> <p>18 BY MS. PARFITT:</p> <p>19 Q Did you read the report?</p> <p>20 A So I -- I'm not sure if I read this one</p> <p>21 with this particular date.</p> <p>22 Q That's fine.</p> <p>23 A But wait, wait, wait. But, you know, if</p> <p>24 it's on here, because that's what it reminds me</p> <p>25 of, I don't have a specific memory for this matter</p>
Page 67	Page 69
<p>1 of November 14th, 2018 --</p> <p>2 Q Correct.</p> <p>3 A -- I know I've seen at least a few of</p> <p>4 Dr. Longo's reports, and I -- I think they're the</p> <p>5 same over and over again. So I -- if I -- if I'm</p> <p>6 not mistaken, I don't think I would have reread it</p> <p>7 like, you know, specifically for this matter if it</p> <p>8 looked the same as others. I think I probably</p> <p>9 just like flipped through it to see what it was --</p> <p>10 was there generally.</p> <p>11 Q All right. So I understand your answer,</p> <p>12 is your testimony that you don't recall</p> <p>13 specifically reviewing the November 14th, 2018</p> <p>14 expert report of Dr. Longo's and Rigler?</p> <p>15 MS. BROWN: Objection to the form,</p> <p>16 misstates his testimony.</p> <p>17 MS. MILLER: So can I say something?</p> <p>18 Because I was involved in that, I think that every</p> <p>19 item with respect to litigation that we sent to</p> <p>20 Dr. Diette, which would have been depositions or</p> <p>21 expert reports, was put on the list because it was</p> <p>22 sent to him. I --</p> <p>23 MS. PARFITT: Oh, and I understand. I</p> <p>24 appreciate that.</p> <p>25 BY MS. PARFITT:</p>	<p>1 because I've been reading some of these things for</p> <p>2 other matters as well. So I -- you know, I don't</p> <p>3 remember whether -- whether I read that particular</p> <p>4 one, but if it looked like other ones that I had,</p> <p>5 I would have, you know, touched it, opened it,</p> <p>6 looked to see what was in there, and then not read</p> <p>7 every word of it. But I don't remember which way</p> <p>8 it worked.</p> <p>9 Q Sitting here today, are you able to tell</p> <p>10 me the results of Dr. Longo and Rigler's testing</p> <p>11 of Johnson & Johnson's talcum powder products as</p> <p>12 reflected in their expert reports of November 14,</p> <p>13 2018?</p> <p>14 MS. BROWN: Objection to the form.</p> <p>15 THE WITNESS: I don't remember the</p> <p>16 details, but I could -- I could look that up and</p> <p>17 pull -- pull out what I saw.</p> <p>18 BY MS. PARFITT:</p> <p>19 Q Did you mark it?</p> <p>20 MS. BROWN: Objection to the form.</p> <p>21 THE WITNESS: Oh, you mean like with</p> <p>22 highlights?</p> <p>23 BY MS. PARFITT:</p> <p>24 Q Mm-hmm. Yes, with highlights.</p> <p>25 A Sorry. I thought you were talking about</p>

18 (Pages 66 to 69)

Gregory B. Diette, M.D.

Page 70	Page 72
<p>1 marking exhibits, I'm thinking like that's not</p> <p>2 what I do. So, no -- so I don't know.</p> <p>3 Q All right.</p> <p>4 A This particular one, I might have</p> <p>5 highlighted an earlier one or -- or even not. And</p> <p>6 the only reason I say that is because his reports</p> <p>7 tend to have an awful lot of like sort of like</p> <p>8 testing data in the -- in the back of it, and</p> <p>9 there's not a lot of like words, you know, to</p> <p>10 read. So there's not a lot to really highlight</p> <p>11 for me. I mean, you know what I mean? It's kind</p> <p>12 of succinct in terms of like the opinion part, and</p> <p>13 then there's a whole bunch of scientific stuff</p> <p>14 that's somebody else's field.</p> <p>15 Q Understood. And I think what I'm</p> <p>16 getting at is for purposes of the opinions you are</p> <p>17 presenting to the jury in this case, are you</p> <p>18 relying on the test results of Dr. Longo's and</p> <p>19 Rigler's that are contained in not only their</p> <p>20 November 14th -- contained in their November 14th,</p> <p>21 2018 report?</p> <p>22 MS. BROWN: And objection.</p> <p>23 Counsel, you said "jury." I assume you</p> <p>24 mean for purposes of this Daubert hearing, is he</p> <p>25 relying on the Rigler and Longo report of</p>	<p>1 wouldn't say I rely on it in the sense that it's</p> <p>2 an underpinning of an opinion or something like</p> <p>3 that.</p> <p>4 Q All right. Do you have an understanding</p> <p>5 then that Drs. Longo and Rigler found the presence</p> <p>6 of asbestos in the talcum powder products they</p> <p>7 tested?</p> <p>8 MS. BROWN: Objection to the form of the</p> <p>9 question.</p> <p>10 THE WITNESS: My -- my understanding is</p> <p>11 they say they found it, but I don't -- I don't</p> <p>12 know the fact of whether they found it or not.</p> <p>13 BY MS. PARFITT:</p> <p>14 Q Okay. Did -- from your read or not read</p> <p>15 of Drs. Longo and Rigler -- strike that.</p> <p>16 Did Drs. Longo and Rigler find</p> <p>17 asbestiform fibers in the tests done of Johnson &</p> <p>18 Johnson's product, talcum powder products?</p> <p>19 MS. BROWN: Objection to the form.</p> <p>20 THE WITNESS: I guess I need to know</p> <p>21 what we're talking about if you say "asbestiform</p> <p>22 fibers," because I thought your question before</p> <p>23 was asbestos.</p> <p>24 BY MS. PARFITT:</p> <p>25 Q It was.</p>
Page 71	Page 73
<p>1 November 14th, 2018.</p> <p>2 BY MS. PARFITT:</p> <p>3 Q For purposes of the opinions that you</p> <p>4 have provided in your expert report and I assume</p> <p>5 will present to Judge Wolfson sometime in July,</p> <p>6 are you relying on the information that's</p> <p>7 contained in the expert report of Dr. Longo and</p> <p>8 Rigler, November 14, 2018?</p> <p>9 A I wouldn't use the word "rely." I would</p> <p>10 say aware of, but not -- I'm not relying on it.</p> <p>11 Q And let me explore that, because this is</p> <p>12 the only time I will have a chance to talk to you</p> <p>13 before that Daubert hearing.</p> <p>14 A Sure.</p> <p>15 Q Are you, for purposes of your opinion</p> <p>16 that you're sharing -- will share with me today</p> <p>17 and will share with the court in July, relying on</p> <p>18 any of the test results of Drs. Longo and Rigler</p> <p>19 contained in their reports of November 14, 2018?</p> <p>20 A Yeah, I think the way I said it is</p> <p>21 exactly right, because to me "rely on" has some --</p> <p>22 there's some legal connotation for that, right.</p> <p>23 And so it doesn't -- it doesn't inform</p> <p>24 my opinion, but I'm aware of what his general</p> <p>25 position has been. And so -- but I don't -- I</p>	<p>1 A And are you expecting me to -- to say</p> <p>2 that that's two different things, or is it just</p> <p>3 another way of you trying to ask the same</p> <p>4 question?</p> <p>5 Q How do you define "asbestiform fibers"?</p> <p>6 MR. LOCKE: Objection.</p> <p>7 MS. BROWN: Objection to the form of the</p> <p>8 question.</p> <p>9 THE WITNESS: Well, I -- I understand</p> <p>10 some the terminology, but I'm not a mineralogist.</p> <p>11 Right. So I -- I can tell you -- I think I have</p> <p>12 to diverge a little bit to answer your question,</p> <p>13 if I can, just to say that -- unless you don't</p> <p>14 want me to. Feel free to --</p> <p>15 MS. BROWN: No, you should answer the</p> <p>16 question --</p> <p>17 THE WITNESS: Okay.</p> <p>18 MS. BROWN: -- as honestly and</p> <p>19 truthfully and accurately as you can.</p> <p>20 THE WITNESS: Because asbestos -- I</p> <p>21 mean, asbestos in terms of at least its</p> <p>22 commercial, you know, forms is something that's</p> <p>23 in -- that's in asbestiform fiber, right. It's in</p> <p>24 asbestiform habit. And so I think, you know, for</p> <p>25 me to understand the minerals, when we're talking</p>

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 74</p> <p>1 about asbestos, we're talking about a particular</p> <p>2 kind of mineral that's in a particular form or</p> <p>3 habit.</p> <p>4 And so I -- I think when you're talking</p> <p>5 about an asbestiform fiber, there's some</p> <p>6 redundancy there in a way, right, which is that</p> <p>7 that's a description that you could apply to</p> <p>8 something that other people would call asbestos.</p> <p>9 BY MS. PARFITT:</p> <p>10 Q All right. Fine. Thank you.</p> <p>11 Has Johnson & Johnson provided you with</p> <p>12 any testing that they performed on their product?</p> <p>13 MS. BROWN: Objection.</p> <p>14 BY MS. PARFITT:</p> <p>15 Q Shower to Shower or Johnson's Baby</p> <p>16 Powder.</p> <p>17 MS. BROWN: Objection.</p> <p>18 THE WITNESS: I don't think I have seen</p> <p>19 anything.</p> <p>20 BY MS. PARFITT:</p> <p>21 Q Did you ever ask Johnson & Johnson to</p> <p>22 see any of the testing that they performed on</p> <p>23 their own talcum powder products?</p> <p>24 MS. BROWN: Objection. Asked and</p> <p>25 answered.</p>	<p style="text-align: right;">Page 76</p> <p>1 would not alter your analysis, and I assume</p> <p>2 opinions, with regard to talcum powder products</p> <p>3 causing ovarian cancer.</p> <p>4 A That's in my report?</p> <p>5 Q Yes.</p> <p>6 A Can we flip to that?</p> <p>7 Q Sure. Why don't you go to page 3.</p> <p>8 And if I may, it's at the bottom,</p> <p>9 paragraph 6.</p> <p>10 A I'm with you, yeah.</p> <p>11 Q Okay. And it says: "To the extent</p> <p>12 plaintiffs' expert opined that asbestos is an</p> <p>13 accessory mineral present in cosmetic talc that</p> <p>14 causes ovarian cancer, this theory would not alter</p> <p>15 the analysis because the existing epidemiological</p> <p>16 literature regarding talc use would</p> <p>17 necessarily" --</p> <p>18 MS. BROWN: You're reading it --</p> <p>19 MS. PARFITT: Beg your pardon?</p> <p>20 MS. BROWN: You read it wrong. Perineal</p> <p>21 talc use.</p> <p>22 MS. PARFITT: Oh, I'm sorry. Perineal.</p> <p>23 Thank you.</p> <p>24 BY MS. PARFITT:</p> <p>25 Q -- "perineal talc use would necessarily</p>
<p style="text-align: right;">Page 75</p> <p>1 THE WITNESS: I have not.</p> <p>2 BY MS. PARFITT:</p> <p>3 Q Okay. Dr. Diette, are you aware that</p> <p>4 there are generic talcum powder products being</p> <p>5 sold in the marketplace today that contain an</p> <p>6 ovarian cancer warning for individuals who use it</p> <p>7 in their genital area?</p> <p>8 MS. BROWN: Objection to the form --</p> <p>9 THE WITNESS: I don't --</p> <p>10 MS. BROWN: -- lacks foundation, calls</p> <p>11 for speculation.</p> <p>12 THE WITNESS: I don't know one way or</p> <p>13 the other.</p> <p>14 BY MS. PARFITT:</p> <p>15 Q Okay. Has Johnson & Johnson shared that</p> <p>16 information with you?</p> <p>17 MS. BROWN: Same objections.</p> <p>18 THE WITNESS: Well, if they had, I'd be</p> <p>19 aware of it, right? I mean --</p> <p>20 BY MS. PARFITT:</p> <p>21 Q I would think.</p> <p>22 A Yeah. So it has to be no. Yeah.</p> <p>23 Q Okay. You state in your -- you state in</p> <p>24 your expert report that the presence of asbestos</p> <p>25 as an accessory mineral present in cosmetic talc</p>	<p style="text-align: right;">Page 77</p> <p>1 account for the presence of any asbestos in the</p> <p>2 products used in both studies."</p> <p>3 Did I now read that correctly, with</p> <p>4 counsel's correction?</p> <p>5 A Yeah, you're -- you've got it right now.</p> <p>6 Q Okay. What do you mean by that</p> <p>7 statement?</p> <p>8 A So what I -- what I mean generally is</p> <p>9 that I've reviewed the -- what I think is the</p> <p>10 whole epidemiology on the -- on the topic, and the</p> <p>11 studies themselves don't break down or don't do</p> <p>12 analyses of what the talcum powder is or what it</p> <p>13 consists of. So to the extent that they've</p> <p>14 studied talcum powder, to me whatever is in talcum</p> <p>15 powder is baked into the epidemiology. And so</p> <p>16 whether asbestos is a fact that it's in there or</p> <p>17 it's a fact that it's not doesn't really change</p> <p>18 how to interpret those studies.</p> <p>19 Is that what you're asking?</p> <p>20 Q Mm-hmm.</p> <p>21 A Okay.</p> <p>22 Q Mm-hmm. Is asbestos a carcinogen?</p> <p>23 A It is.</p> <p>24 Q We're going to come back to that.</p> <p>25 Let me just get on a little bit further</p>

Gregory B. Diette, M.D.

Page 78	Page 80
<p>1 on here.</p> <p>2 Are you going to be giving an opinion in</p> <p>3 this case that Johnson & Johnson's talcum powder</p> <p>4 products contain asbestos?</p> <p>5 A No.</p> <p>6 Q You will not?</p> <p>7 A I will not.</p> <p>8 Q Have you made an assumption then for</p> <p>9 purposes of your opinion that Johnson's -- that</p> <p>10 Johnson & Johnson's talcum powder products do not</p> <p>11 contain asbestos?</p> <p>12 A I -- no, I haven't made that assumption.</p> <p>13 I -- I recognize that there's a debate about that,</p> <p>14 and I don't have the expertise to sort through</p> <p>15 what's right about that debate.</p> <p>16 Q All right. Assume that Johnson &</p> <p>17 Johnson's talcum powder products contain asbestos,</p> <p>18 would that place consumers that use the product in</p> <p>19 needless danger?</p> <p>20 MS. BROWN: Objection. Counsel, that's</p> <p>21 an incomplete hypothetical. Is that the same talc</p> <p>22 that's in the epi?</p> <p>23 BY MS. PARFITT:</p> <p>24 Q Can you answer the question?</p> <p>25 MS. PARFITT: And please don't coach the</p>	<p>1 all over the world, right. And so everything</p> <p>2 comes down to dose in any case, right. So for me</p> <p>3 to be concerned about it, you'd have to show me</p> <p>4 that there's a sufficient dose that a person gets</p> <p>5 in order to raise the risk of whatever it is that</p> <p>6 you're talking about.</p> <p>7 BY MS. PARFITT:</p> <p>8 Q Let me ask you this: Assume Johnson &</p> <p>9 Johnson's talcum powder products has asbestos in</p> <p>10 it. Are you with me?</p> <p>11 A I am, yeah.</p> <p>12 Q All right. Would it be imprudent for</p> <p>13 Johnson & Johnson to sell its talcum powder</p> <p>14 products to consumers to use it in their</p> <p>15 genital -- on their genital areas?</p> <p>16 MS. BROWN: I object to this line of</p> <p>17 question, Counsel. Are you divorcing your</p> <p>18 hypothetical from the epidemiology he has reviewed</p> <p>19 and is here to talk about?</p> <p>20 MS. PARFITT: He didn't answer the</p> <p>21 question, Counsel. Counsel, if he understands --</p> <p>22 he understood the last question, it's the same.</p> <p>23 Thank you.</p> <p>24 MS. BROWN: I object to the entire line</p> <p>25 of questioning.</p>
Page 79	Page 81
<p>1 witness.</p> <p>2 MS. BROWN: Objection to the incomplete</p> <p>3 hypothetical.</p> <p>4 THE WITNESS: So, anyway, so the</p> <p>5 needless part, I think -- I'm not sure if you need</p> <p>6 that in your question or whether it changes how I</p> <p>7 would answer it. I think the general issue is</p> <p>8 whether or not there's a risk or whether there's a</p> <p>9 danger. And from what I can tell from reading the</p> <p>10 literature, that there's not a risk of -- did you</p> <p>11 say "ovarian cancer" in your question?</p> <p>12 BY MS. PARFITT:</p> <p>13 Q Correct.</p> <p>14 A Yeah, I don't see that there's a -- a</p> <p>15 risk of ovarian cancer from the literature.</p> <p>16 Q Assume for purposes of my question that</p> <p>17 Johnson & Johnson's talcum powder products has</p> <p>18 asbestos in it, would it be imprudent and not</p> <p>19 reasonable for Johnson & Johnson to sell that</p> <p>20 product to its customers, yes or no?</p> <p>21 MS. BROWN: Objection to the incomplete</p> <p>22 hypothetical.</p> <p>23 THE WITNESS: So I think, you know, it</p> <p>24 isn't a yes or no, right? I mean, because it's --</p> <p>25 if you're talking about asbestos, there's asbestos</p>	<p>1 BY MS. PARFITT:</p> <p>2 Q Please.</p> <p>3 A If we're talking about what exists in</p> <p>4 the world right now, I -- I don't see any issue</p> <p>5 with it.</p> <p>6 Q All right. Do you know who</p> <p>7 Dr. Nicholson is?</p> <p>8 A Which -- which Nicholson?</p> <p>9 Q Susan Nicholson.</p> <p>10 A I'm not sure. Is she an expert in --</p> <p>11 Q She's not. She's actually the -- and</p> <p>12 I'll represent to you, the chief medical officer</p> <p>13 for Johnson & Johnson.</p> <p>14 A Oh, I don't know her.</p> <p>15 Q Okay. Let me represent to you that</p> <p>16 Dr. Nicholson, who is a medical officer for</p> <p>17 Johnson & Johnson, was deposed in this case, this</p> <p>18 same case that we're in together, you and I. Are</p> <p>19 you aware of that?</p> <p>20 A Only because you said so.</p> <p>21 Q Okay. And the deposition that was taken</p> <p>22 of Dr. Nicholson was a deposition that was taken</p> <p>23 wherein she -- we call it a 30(b)(6). That means</p> <p>24 she represents the voice of the company that she</p> <p>25 works for. Understand?</p>

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 82</p> <p>1 MS. BROWN: Objection to the form of the</p> <p>2 question.</p> <p>3 THE WITNESS: I understand what you</p> <p>4 said. I don't know what I -- if I understand what</p> <p>5 that means.</p> <p>6 MS. PARFITT: Okay. All right. Let me</p> <p>7 have marked as Exhibit -- I believe it's</p> <p>8 Exhibit No. 6 that we're on.</p> <p>9 (Diette Exhibit No. 6 was marked</p> <p>10 for identification.)</p> <p>11 MS. BROWN: And, Counsel, if you're</p> <p>12 going to ask him questions about Dr. Nicholson's</p> <p>13 deposition that he has not reviewed, we need to at</p> <p>14 least have a full copy of the deposition here.</p> <p>15 Thanks.</p> <p>16 MS. PARFITT: I believe you have --</p> <p>17 MS. BROWN: And you should take as long</p> <p>18 as you need to review it to answer any questions</p> <p>19 counsel might have.</p> <p>20 MS. PARFITT: Okay. And, Counsel, I'll</p> <p>21 get you that -- I don't have a copy --</p> <p>22 MS. BROWN: We have -- I mean your</p> <p>23 colleague just --</p> <p>24 MS. PARFITT: We have just one. I'm</p> <p>25 just saying we just have one. I don't have one</p>	<p style="text-align: right;">Page 84</p> <p>1 Q Okay. At the top, if I may, it says --</p> <p>2 line 2: "Well" -- and I'll represent to you that</p> <p>3 I was one of the attorneys that took</p> <p>4 Dr. Nicholson's deposition.</p> <p>5 The question is: "Well, if your</p> <p>6 products contain asbestos, would you agree with me</p> <p>7 that that impacts the safety of the product?"</p> <p>8 Answer: "Absolutely, yes."</p> <p>9 Next question: "Would you agree that</p> <p>10 Johnson & Johnson has a zero tolerance policy with</p> <p>11 regard to having asbestos in their talcum powder</p> <p>12 products?"</p> <p>13 The answer: "Yeah, that is correct."</p> <p>14 Next question: "In fact, as a</p> <p>15 representative of the company, it's your position</p> <p>16 that your Johnson & Johnson's talcum powder</p> <p>17 products should not contain asbestos; is that</p> <p>18 correct?"</p> <p>19 "That's correct -- that is correct."</p> <p>20 Next question: "And you would agree</p> <p>21 with me that if your talcum powder products had</p> <p>22 asbestos in them, it would place the consumers</p> <p>23 that use your product in needless danger,</p> <p>24 correct?"</p> <p>25 "It could, yes."</p>
<p style="text-align: right;">Page 83</p> <p>1 for you.</p> <p>2 MS. BROWN: As long as the doctor has</p> <p>3 time to review it -- you know he hasn't seen this</p> <p>4 before. If you're going to ask him questions</p> <p>5 about it, he needs to read it.</p> <p>6 MS. PARFITT: Just one.</p> <p>7 BY MS. PARFITT:</p> <p>8 Q Dr. Nich- -- or Dr. Diette, let me</p> <p>9 direct your attention to page 37.</p> <p>10 A Okay.</p> <p>11 Q And specifically line 2, and let me read</p> <p>12 it. We'll put it up on the ELMO.</p> <p>13 MS. BROWN: Counsel, while you're doing</p> <p>14 that, I'm going to object to taking one page out</p> <p>15 of Dr. Nicholson's deposition that the doctor has</p> <p>16 not reviewed and asking questions out of context.</p> <p>17 And if he needs to read the whole deposition to</p> <p>18 answer your question, he will need to do that.</p> <p>19 MS. PARFITT: Counsel, please not --</p> <p>20 let's not coach.</p> <p>21 MS. BROWN: And I'm objecting on the</p> <p>22 record to the improper questioning with snippets</p> <p>23 of somebody else's deposition.</p> <p>24 MS. PARFITT: Okay.</p> <p>25 BY MS. PARFITT:</p>	<p style="text-align: right;">Page 85</p> <p>1 Next question on page 48 of that same</p> <p>2 deposition --</p> <p>3 MS. BROWN: Counsel, I'm sorry, but your</p> <p>4 pages are not matching up to what we've been</p> <p>5 handed. Can you just direct us -- and we're -- in</p> <p>6 the snippet you gave us, I can't find this.</p> <p>7 THE WITNESS: I don't have 48. Mine</p> <p>8 goes to 41.</p> <p>9 MS. BROWN: Yeah, mine says 37, 37, 37.</p> <p>10 THE WITNESS: Maybe here in the whole</p> <p>11 thing?</p> <p>12 MR. HEASLIP: And mine is 46 through 53.</p> <p>13 MS. PARFITT: Okay.</p> <p>14 MS. BROWN: This is not what you're</p> <p>15 reading, so it's impossible to follow.</p> <p>16 Were you able to follow that, Doctor?</p> <p>17 MS. PARFITT: We have it on the</p> <p>18 overhead. I think --</p> <p>19 MR. ROSEN: I go to -- I go to 41.</p> <p>20 MS. BROWN: Yeah, well, he needs to have</p> <p>21 it in front of him. We don't have a copy.</p> <p>22 MS. PARFITT: Well, let's do this. I</p> <p>23 have an overhead and an ELMO. So let's keep</p> <p>24 going. Why don't you read the screen.</p> <p>25 Do you need me to go back over those</p>

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 86</p> <p>1 questions?</p> <p>2 MS. BROWN: But, Counsel, that's not</p> <p>3 even a transcript. What is that?</p> <p>4 MS. PARFITT: It's --</p> <p>5 MS. MILLER: How are you going to mark</p> <p>6 that as an exhibit?</p> <p>7 MS. PARFITT: I'm going to put an</p> <p>8 exhibit sticker on it, and I'm going to put it in</p> <p>9 as representative pages from the Nicholson</p> <p>10 deposition.</p> <p>11 MS. BROWN: Can he find it in the large</p> <p>12 copy?</p> <p>13 MR. ROSEN: Would you mind passing</p> <p>14 back Exhibit 6 that we handed --</p> <p>15 THE WITNESS: Oh. This is all of your</p> <p>16 36's. That's a whole bundle of the same thing.</p> <p>17 But I would like to get the 36-page</p> <p>18 back --</p> <p>19 MS. PARFITT: Sure.</p> <p>20 THE WITNESS: -- if we're going to talk</p> <p>21 about it.</p> <p>22 MS. PARFITT: Absolutely. I want you to</p> <p>23 have actually 37, and you need -- here we go.</p> <p>24 MS. BROWN: This is the complete set?</p> <p>25 MS. PARFITT: Yes, I'm assuming.</p>	<p style="text-align: right;">Page 88</p> <p>1 Did I read all that correctly?</p> <p>2 A You did.</p> <p>3 Q All right. Do you -- so you disagree</p> <p>4 with Dr. Nicholson; is that correct?</p> <p>5 MS. BROWN: Objection to the form.</p> <p>6 MR. LOCKE: Objection.</p> <p>7 MS. BROWN: Misstates his testimony.</p> <p>8 THE WITNESS: I don't -- I don't agree</p> <p>9 or disagree. I mean, I -- I honestly don't know</p> <p>10 who she is other than what you just said. But --</p> <p>11 but it sounds like she's articulating a policy for</p> <p>12 the company, which I think is her right -- her</p> <p>13 right to do that and to express those opinions.</p> <p>14 BY MS. PARFITT:</p> <p>15 Q Okay. All right.</p> <p>16 Okay. Now, counsel provided for us in</p> <p>17 advance of this deposition a copy of your CV. So</p> <p>18 let me --</p> <p>19 THE WITNESS: Would it -- would it be a</p> <p>20 good time just to refill coffee? Is that okay?</p> <p>21 MS. PARFITT: Sure. And I should have</p> <p>22 said that. Any time you need a break --</p> <p>23 THE WITNESS: No, I know.</p> <p>24 MS. PARFITT: -- you holler.</p> <p>25 THE WITNESS: Thank you. I appreciate</p>
<p style="text-align: right;">Page 87</p> <p>1 MS. BROWN: You have that in front of</p> <p>2 you?</p> <p>3 THE WITNESS: I do.</p> <p>4 BY MS. PARFITT:</p> <p>5 Q And, Dr. Diette, if you have any trouble</p> <p>6 reading any of that -- or you can also look up on</p> <p>7 the ELMO that's being displayed.</p> <p>8 MS. BROWN: Thank you.</p> <p>9 MS. PARFITT: Okay. Yeah, sorry.</p> <p>10 BY MS. PARFITT:</p> <p>11 Q Again, page 48, line 14.</p> <p>12 Do you have that there, Doctor, in front</p> <p>13 of you?</p> <p>14 A I do.</p> <p>15 Q Okay.</p> <p>16 "Q. You would agree, Dr. Nicholson, if</p> <p>17 Johnson & Johnson's Baby Powder indeed had</p> <p>18 asbestos in it, it would be imprudent and not</p> <p>19 reasonable for Johnson & Johnson to sell it to its</p> <p>20 consumers?"</p> <p>21 "A. I would agree with that.</p> <p>22 "Q. Thank you.</p> <p>23 "A. I would not support Johnson &</p> <p>24 Johnson selling a product that contained</p> <p>25 asbestos."</p>	<p style="text-align: right;">Page 89</p> <p>1 that.</p> <p>2 MS. PARFITT: You're very welcome.</p> <p>3 THE VIDEOGRAPHER: The time is 10:07</p> <p>4 p.m. We're going off the record.</p> <p>5 (Recess.)</p> <p>6 THE VIDEOGRAPHER: The time is</p> <p>7 10:20 a.m., and we're back on the record.</p> <p>8 BY MS. PARFITT:</p> <p>9 Q Dr. Diette, are you still --</p> <p>10 THE VIDEOGRAPHER: Microphone, Counsel.</p> <p>11 BY MS. PARFITT:</p> <p>12 Q Are you good?</p> <p>13 A All set. Thank you.</p> <p>14 Q All right. Dr. Diette, if asbestos was</p> <p>15 found to be in talcum powder products -- strike</p> <p>16 that.</p> <p>17 Would the presence of asbestos in talcum</p> <p>18 powder products provide evidence to support the</p> <p>19 hypothesis that talcum powder products -- strike</p> <p>20 that.</p> <p>21 Would the presence of asbestos in talcum</p> <p>22 powder products provide biologically plausible</p> <p>23 evidence to support the hypothesis that talcum</p> <p>24 powder products can cause ovarian cancer?</p> <p>25 MR. LOCKE: Objection.</p>

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 90</p> <p>1 MS. BROWN: Objection to the form of the</p> <p>2 question.</p> <p>3 THE WITNESS: You would have to qualify</p> <p>4 it, right, because I -- if you're talking about</p> <p>5 like -- even like, you know, one fiber or</p> <p>6 something would be quite different than if there's</p> <p>7 a sufficient amount in order to -- to cause a</p> <p>8 disease, right. So it -- it always comes down to</p> <p>9 dose in terms of what you're talking about.</p> <p>10 So it's -- all by itself, I don't think</p> <p>11 that that question is answerable.</p> <p>12 BY MS. PARFITT:</p> <p>13 Q Can one fiber of asbestos alone cause</p> <p>14 cancer?</p> <p>15 MS. BROWN: Objection to the form.</p> <p>16 THE WITNESS: It's -- it's so impossible</p> <p>17 to think that it would, because we all have</p> <p>18 asbestos in our lungs, and there's a background</p> <p>19 amount of asbestos in the world that if one fiber</p> <p>20 could do it, I think we would all have cancer. So</p> <p>21 I -- I think somebody could say that, but I don't</p> <p>22 think it would be true.</p> <p>23 BY MS. PARFITT:</p> <p>24 Q You certainly don't think it's true; is</p> <p>25 that correct?</p>	<p style="text-align: right;">Page 92</p> <p>1 papers that have been either accepted or published</p> <p>2 since then. There's probably some talks and</p> <p>3 things. The -- the grant award section I'm sure</p> <p>4 needs updating.</p> <p>5 Q Okay. It looks, on the far right of</p> <p>6 that CV, that it's got a June 2017 date; is that</p> <p>7 correct?</p> <p>8 A It is.</p> <p>9 Q All right. Has there been a curriculum</p> <p>10 vitae prepared by you since June of 2017?</p> <p>11 A No.</p> <p>12 Q All right. Where would I get these</p> <p>13 additional articles and speeches? Do you have</p> <p>14 them in a -- contained in one particular place?</p> <p>15 A No. Where -- where you could get the</p> <p>16 articles would be on PubMed, and if you just did a</p> <p>17 PubMed search with my name, you would find them</p> <p>18 all.</p> <p>19 For speeches, I don't actually have a</p> <p>20 repository, so it's going to take me some work to</p> <p>21 actually sort of populate that part of the CV.</p> <p>22 Q Are you -- do you have any intention of</p> <p>23 updating your CV?</p> <p>24 A Yes. Can I give you an extra sentence</p> <p>25 or two?</p>
<p style="text-align: right;">Page 91</p> <p>1 A Oh, for sure, yeah.</p> <p>2 Q Okay. Let me mark at this time a</p> <p>3 copy -- a copy of your curriculum vitae, and we'll</p> <p>4 have it marked as exhibit -- Exhibit 7.</p> <p>5 (Diette Exhibit No. 7 was marked</p> <p>6 for identification.)</p> <p>7 BY MS. PARFITT:</p> <p>8 Q Do you have that in front of you?</p> <p>9 A I do.</p> <p>10 Q Okay. Who prepared that curriculum</p> <p>11 vitae?</p> <p>12 A Well, not one person. This is an</p> <p>13 iterative exercise over time. So it's -- I mean,</p> <p>14 me in the sense, although not as the person, you</p> <p>15 know, typing the words, but it's -- you know, it's</p> <p>16 my -- my information on here. And I've had</p> <p>17 different administrative assistants who have --</p> <p>18 who have helped to sort of shape it.</p> <p>19 Q Is it current?</p> <p>20 A No.</p> <p>21 Q It's not?</p> <p>22 A It's not.</p> <p>23 Q All right. What additions or deletions</p> <p>24 would you make to your curriculum vitae?</p> <p>25 A For the most part, I'd add a bunch of</p>	<p style="text-align: right;">Page 93</p> <p>1 Q Sure.</p> <p>2 A Okay. So I sure want to. The stakes</p> <p>3 are low for me at this point. This is our</p> <p>4 Department of Medicine format CV, which we use for</p> <p>5 promotion purposes, for the most part. I've been</p> <p>6 promoted to professor, which there's no other rank</p> <p>7 to get promoted to. And so it's not really that</p> <p>8 urgent for me to -- to change that.</p> <p>9 Then on top of that, my administrative</p> <p>10 assistant went out on maternity leave, and then I</p> <p>11 didn't want to swamp her with this when she came</p> <p>12 back.</p> <p>13 Q That was nice.</p> <p>14 A And literally just last week, she took a</p> <p>15 new job, a better job but in a different place.</p> <p>16 So long answer, yeah, I want to, but</p> <p>17 it's not going to happen really soon.</p> <p>18 Q Okay. So your current academic</p> <p>19 appointment at Johns Hopkins University, is that a</p> <p>20 professor of medicine, is that correct, Division</p> <p>21 of Pulmonary and Critical Care?</p> <p>22 A Yeah, and I think it's called Pulmonary,</p> <p>23 Criteria Care and Sleep Medicine now. We just --</p> <p>24 we just changed the name recently.</p> <p>25 Q And sleep medicine?</p>

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 94</p> <p>1 A And sleep, yeah.</p> <p>2 Q All right. Are you still within the</p> <p>3 Department of Epidemiology?</p> <p>4 A Yes.</p> <p>5 Q All right. Are you still an associate</p> <p>6 professor of medicine in epi and environmental</p> <p>7 health?</p> <p>8 A No, that's a typo somewhere. I don't</p> <p>9 know where you saw that, but -- oh, probably in my</p> <p>10 report. But, no, I'm -- the professor label</p> <p>11 carries across all the -- the different entities.</p> <p>12 Q So you're no longer an associate</p> <p>13 professor.</p> <p>14 A Right. Professor of whatever it is that</p> <p>15 I'm a professor of.</p> <p>16 Q All right. Your board certification is</p> <p>17 in pulmonary and critical care?</p> <p>18 A It's in internal medicine and pulmonary</p> <p>19 medicine.</p> <p>20 Q You're not a member of the American</p> <p>21 College of Epidemiology, correct?</p> <p>22 A No.</p> <p>23 Q Your undergraduate degree was in</p> <p>24 English?</p> <p>25 A English and economics.</p>	<p style="text-align: right;">Page 96</p> <p>1 hospital as well.</p> <p>2 Q All right. So if someone were going on</p> <p>3 the website to look at the hospital, the medical</p> <p>4 school, medical center, this is what they would</p> <p>5 see. And look over to the far right, and it has</p> <p>6 "Expertise." Do you see that?</p> <p>7 A I do.</p> <p>8 Q All right. Is -- it reads: "Expertise:</p> <p>9 Asthma, chronic obstructive pulmonary disease</p> <p>10 (COPD), pulmonary" -- excuse me -- "pulmonary</p> <p>11 disease, and critical care medicine, pulmonary</p> <p>12 medicine."</p> <p>13 Is that correct?</p> <p>14 A It is correct.</p> <p>15 Q All right. Is there anything you want</p> <p>16 to add with regard to your expertise?</p> <p>17 MS. BROWN: Objection to the form of the</p> <p>18 question.</p> <p>19 THE WITNESS: So I honestly don't know</p> <p>20 what this is. I mean, I don't doubt that it comes</p> <p>21 from Hopkins, but it's not something I look at.</p> <p>22 BY MS. PARFITT:</p> <p>23 Q Okay.</p> <p>24 A If you -- well, no, just one second.</p> <p>25 Because if you look at the bottom, it says</p>
<p style="text-align: right;">Page 95</p> <p>1 Q Okay. And then post-medical school, you</p> <p>2 received a MHS in public health; is that correct?</p> <p>3 A Well, it was in epidemiology.</p> <p>4 Q Okay.</p> <p>5 A I only just say that because there is a</p> <p>6 degree in public health, and that's not what mine</p> <p>7 was called.</p> <p>8 Q Okay. Let me show you what we'll have</p> <p>9 marked as the Johns Hopkins Medicine website as --</p> <p>10 MS. PARFITT: What exhibit?</p> <p>11 MS. BROWN: 8.</p> <p>12 BY MS. PARFITT:</p> <p>13 Q -- Exhibit 8?</p> <p>14 (Diette Exhibit No. 8 was marked</p> <p>15 for identification.)</p> <p>16 BY MS. PARFITT:</p> <p>17 Q All right. Do you have that in front of</p> <p>18 you?</p> <p>19 A I do.</p> <p>20 Q All right. Now, this is for the Johns</p> <p>21 Hopkins Medical School; is that correct, or</p> <p>22 medical center?</p> <p>23 A So I don't know. You know, the top says</p> <p>24 "Johns Hopkins Medicine," which is a broader label</p> <p>25 that includes the medical school and probably the</p>	<p style="text-align: right;">Page 97</p> <p>1 "Request an appointment." So this looks like some</p> <p>2 kind of place that somebody could go and find a</p> <p>3 call-in number to get an appointment for -- for a</p> <p>4 doctor.</p> <p>5 Q Okay.</p> <p>6 A So I think it's -- I don't know. I</p> <p>7 could add all kinds of things, but I don't -- I</p> <p>8 don't know what the format is for this. Like I</p> <p>9 don't know if there is a word limit.</p> <p>10 Q Sorry.</p> <p>11 A I don't know -- I don't know what the</p> <p>12 purpose of this is.</p> <p>13 Q All right. The second line says:</p> <p>14 "Research interests," and it states:</p> <p>15 "Environmental impacts on lung disease,</p> <p>16 epidemiology of airway disease and chronic</p> <p>17 obstructive pulmonary disease, asthma."</p> <p>18 Did I read that correctly?</p> <p>19 A You did.</p> <p>20 Q Does that accurately reflect your</p> <p>21 current research interests?</p> <p>22 MS. BROWN: Objection. Form.</p> <p>23 THE WITNESS: Well, it's some, but it's</p> <p>24 so incomplete. You know, it's obviously just a</p> <p>25 couple of snippets that somebody chose to put on</p>

Gregory B. Diette, M.D.

Page 98	Page 100
<p>1 this -- on this page.</p> <p>2 BY MS. PARFITT:</p> <p>3 Q Okay. Well, I will represent to you</p> <p>4 that if one chose to go on the Johns Hopkins</p> <p>5 Medicine website, this is how they hold you out to</p> <p>6 the -- to the world, so to speak.</p> <p>7 MS. BROWN: Objection to the speech. Is</p> <p>8 there a question?</p> <p>9 THE WITNESS: So --</p> <p>10 MS. PARFITT: Counsel --</p> <p>11 MS. BROWN: There's no question.</p> <p>12 MS. PARFITT: -- please.</p> <p>13 MS. BROWN: Is there a question?</p> <p>14 MS. PARFITT: Yes.</p> <p>15 MS. BROWN: What is it?</p> <p>16 BY MS. PARFITT:</p> <p>17 Q Is this how -- is this information</p> <p>18 correct, Dr. Diette?</p> <p>19 A Oh, the information is correct.</p> <p>20 Q Okay.</p> <p>21 A It's very incomplete.</p> <p>22 Q Okay. Let me show you now what we'll</p> <p>23 have marked as Exhibit 9.</p> <p>24 (Diette Exhibit No. 9 was marked</p> <p>25 for identification.)</p>	<p>1 it to see if it's accurate or not, but there's --</p> <p>2 there's certainly more about me than just those</p> <p>3 couple of --</p> <p>4 Q Okay. Well, you know, that's a good</p> <p>5 point, and I missed that. So thank you for</p> <p>6 bringing that to our attention.</p> <p>7 Let's look at that sec- -- second page</p> <p>8 of the website for Johns Hopkins Medical Center.</p> <p>9 MR. TISI: Counsel, that is Exhibit 8.</p> <p>10 MS. PARFITT: And it is Exhibit 8.</p> <p>11 Thank you.</p> <p>12 Okay. Let's put that up there.</p> <p>13 BY MS. PARFITT:</p> <p>14 Q And there's a category that says</p> <p>15 "Background"; is that correct?</p> <p>16 A It is.</p> <p>17 Q All right. Now, it states:</p> <p>18 "Dr. Gregory Diette is a professor of medicine at</p> <p>19 the Johns Hopkins University School of Medicine.</p> <p>20 He holds a joint appointment in the Department of</p> <p>21 Epidemiology in the Johns Hopkins Bloomberg School</p> <p>22 of Public Health." Hashtag, "His areas of</p> <p>23 clinical expertise include asthma and obstructive</p> <p>24 lung disease."</p> <p>25 Did I read that correctly?</p>
Page 99	Page 101
<p>1 THE WITNESS: Can I just -- just</p> <p>2 clarify?</p> <p>3 BY MS. PARFITT:</p> <p>4 Q There's no question pending right now.</p> <p>5 A I want to clarify my last --</p> <p>6 MS. BROWN: But if you want --</p> <p>7 BY MS. PARFITT:</p> <p>8 Q Your counsel will have a chance to -- to</p> <p>9 talk with you.</p> <p>10 MS. BROWN: Whoa, Counsel. Are you</p> <p>11 going to take the position on the record that the</p> <p>12 witness can't clarify any --</p> <p>13 MS. PARFITT: No, I'm not doing that</p> <p>14 all.</p> <p>15 MS. BROWN: Well, that was his request,</p> <p>16 and he wanted to --</p> <p>17 BY MS. PARFITT:</p> <p>18 Q What do you need to do, Doctor? I'm</p> <p>19 sorry.</p> <p>20 A Oh, well, I just -- because we were</p> <p>21 talking about this front page, and I didn't</p> <p>22 realize there were other pages here. This still</p> <p>23 isn't complete, but there's a whole lot here more</p> <p>24 about me than just what was on that front page. I</p> <p>25 just wanted to point to all that. I haven't read</p>	<p>1 A You did.</p> <p>2 Q Okay. Is that correct?</p> <p>3 A That -- that it includes those two</p> <p>4 diseases?</p> <p>5 Q Yes.</p> <p>6 A It does include that.</p> <p>7 Q Okay. And the third paragraph reads:</p> <p>8 "His research interests include environmental</p> <p>9 impacts on lung disease, epidemiology of airway</p> <p>10 disease, and chronic obstructive pulmonary</p> <p>11 disease."</p> <p>12 Did I read that correctly?</p> <p>13 A You did.</p> <p>14 Q All right. And does that reflect some</p> <p>15 of your research interests?</p> <p>16 A It does.</p> <p>17 Q All right. Now, let's move over -- and</p> <p>18 thank you for correcting me on that.</p> <p>19 Now, I will represent to you that</p> <p>20 Exhibit 9 is from the website from the Bloomberg</p> <p>21 School of Public Health.</p> <p>22 Do you have that in front of you?</p> <p>23 A I do.</p> <p>24 Q All right. Now, if one was to go onto</p> <p>25 the website for the Bloomberg School of Public</p>

26 (Pages 98 to 101)

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 102</p> <p>1 Health, this is the type of information they would 2 receive, Dr. Diette. 3 Look down at the "Overview." Do you see 4 that? 5 A I do. 6 Q Okay. It says -- 7 MS. PARFITT: Let's get that up on the 8 ELMO. 9 BY MS. PARFITT: 10 Q All right. Do you see under "Overview," 11 it says: "My research focuses on identifying 12 factors that cause or provoke asthma. We have 13 been interested especially in air pollutants," 14 parens, "particulate matter, NO2, secondhand 15 smoke," close parens, "and allergens," parens, 16 "including mouse," close parens, "that are 17 especially problematic in inner city homes. We 18 are studying the effects of these pollutants and 19 allergens on inflammation and oxidative stress. 20 More recently, we have begun examining how dietary 21 patterns, especially a Western diet style -- a 22 Western-style diet, may increase susceptibility to 23 inhalable pollutants and allergens." 24 Did I read that correctly? 25 A You did.</p>	<p style="text-align: right;">Page 104</p> <p>1 patients who come to you are experiencing? 2 MS. BROWN: Objection to the form. 3 THE WITNESS: And I'll do my best, and 4 then if it's not what you're looking for, please 5 just ask me to clarify. 6 I -- I see probably, you know, almost 7 every single kind of medical problem there is 8 because I -- I attend in so many different 9 locations within the Hopkins system. So meaning 10 that I do work in the intensive care unit where 11 it's every kind of medical problem you could 12 imagine, it just happens to be the sickest of the 13 sick. So it could be any -- any organ system, or 14 not even an organ system, but all sorts of 15 illnesses. 16 In the pulmonary clinic, I see -- I 17 certainly see people with asthma and COPD, but I 18 see pretty much any kind of pulmonary disease and 19 get referrals for things that aren't pulmonary 20 diseases. They -- they may be somebody who's got 21 a -- a symptom that turns out not to be a 22 pulmonary disease. 23 In the oncology center, when I attend 24 there, I see every kind of cancer patient that at 25 least that Hopkins sees.</p>
<p style="text-align: right;">Page 103</p> <p>1 Q Okay. And then again, under your 2 "Research Interests, it states: "Epidemiology of 3 lung diseases, asthma, COPD" -- 4 And what's COPD? 5 A Chronic obstructive pulmonary disease. 6 Q -- "outcomes, environmental," and then 7 it says, "Particulate matter, allergens and health 8 disparities." 9 Did I read that correctly? 10 A You did. 11 Q All right. Does that represent some of 12 your research interests? 13 A It does represent some. 14 Q Okay. You are a clinician? 15 A True. 16 Q All right. What is the profile of the 17 types of patients that you see in your practice? 18 MS. BROWN: Form. 19 THE WITNESS: You want me to just take a 20 stab at it? Because I'm not sure -- is profile -- 21 MS. BROWN: If you don't understand the 22 question, I'm sure counsel will clarify it. 23 MS. PARFITT: I will, sure. 24 BY MS. PARFITT: 25 Q What is the nature of the diseases that</p>	<p style="text-align: right;">Page 105</p> <p>1 And then I'm also lucky enough to attend 2 on the general internal medicine service, and so 3 there it's really everything, it's all comers. 4 And so it ranges from basically head-to-toe kind 5 of medicine. 6 BY MS. PARFITT: 7 Q Okay. Now, if I arrived at -- for in -- 8 I guess you said the intensive care clinic, and I 9 had a gynecological problem, would I see you? 10 MS. BROWN: Objection to the form. 11 THE WITNESS: So there's no intensive 12 care clinic, just to be clear. Like a clinic is 13 an outpatient setting. So our intensive care unit 14 is an inpatient setting for critically ill people. 15 BY MS. PARFITT: 16 Q Okay. 17 A So you might or might not end up seeing 18 me, because if we're -- the way that the program 19 works is that -- so, for example, if somebody is 20 pregnant, just giving an example, if it's an early 21 pregnancy, then those patients would end up in our 22 medical ICU. If it's a later pregnancy, then they 23 would go to the -- the obstetrics unit to their -- 24 their own particular unit. And then you might see 25 me if I was consulted into that unit, whether or</p>

Gregory B. Diette, M.D.

Page 106	Page 108
<p>1 not you were in our -- our unit or not.</p> <p>2 Q So if I came in with a gynecological</p> <p>3 problem, they might call you -- you, who are a</p> <p>4 pulmonologist, they might call you in to consult</p> <p>5 with me?</p> <p>6 MS. BROWN: Objection to the form of the</p> <p>7 question and the tone.</p> <p>8 THE WITNESS: Well, I am picking up the</p> <p>9 tone, which I -- which I think -- I mean, I know</p> <p>10 you're trying to make a point here. And the</p> <p>11 question as you asked it is -- the answer is, of</p> <p>12 course. But I think what you're trying to get at</p> <p>13 is would they have asked me to come deal with</p> <p>14 their pregnancy, for example, and I wouldn't be</p> <p>15 the person dealing with their pregnancy. I would</p> <p>16 be dealing with something else.</p> <p>17 BY MS. PARFITT:</p> <p>18 Q Okay. All right. Is it fair to say</p> <p>19 that your practice primarily deals with</p> <p>20 individuals who have pulmonary and lung disease</p> <p>21 conditions?</p> <p>22 MS. BROWN: Objection.</p> <p>23 THE WITNESS: I think if you dial back</p> <p>24 and listen to what I said for those other answers,</p> <p>25 you would be pretty clear that it isn't just that.</p>	<p>1 certainly interested in pollutants.</p> <p>2 Q Okay. And more recently, you've</p> <p>3 expressed a research interest in dietary patterns</p> <p>4 particularly, and especially a Western diet and</p> <p>5 how that might increase susceptibility to</p> <p>6 inhalable pollutants; is that correct?</p> <p>7 A True.</p> <p>8 MS. BROWN: Form.</p> <p>9 BY MS. PARFITT:</p> <p>10 Q Are you -- have you published recently</p> <p>11 on that?</p> <p>12 A I'm sure there's stuff that's come out.</p> <p>13 Q Well, I only have your CV from 2017, so</p> <p>14 I'll represent that I'm not seeing something on</p> <p>15 that CV.</p> <p>16 Is there something you've done recently?</p> <p>17 A Yeah, it's a couple of years ago.</p> <p>18 Q Okay.</p> <p>19 A I mean the best way to find stuff would</p> <p>20 be on PubMed.</p> <p>21 Q All right. You've been retained to</p> <p>22 serve as an expert for Johnson & Johnson, correct?</p> <p>23 MS. BROWN: Form.</p> <p>24 THE WITNESS: That's correct.</p> <p>25 BY MS. PARFITT:</p>
Page 107	Page 109
<p>1 BY MS. PARFITT:</p> <p>2 Q Okay. Well, I would include asthma in</p> <p>3 that as well.</p> <p>4 MS. BROWN: Same objection.</p> <p>5 THE WITNESS: Well, include it, but I</p> <p>6 mean -- but, you know, when I'm on the general</p> <p>7 internal medicine service, I'm not seeing mostly</p> <p>8 asthma. I might be seeing somebody with diabetes</p> <p>9 or a heart attack or pelvic inflammatory disease,</p> <p>10 you know, to name a GYN problem. I mean it's the</p> <p>11 whole gamut from head to toe.</p> <p>12 BY MS. PARFITT:</p> <p>13 Q Is it fair to say your research in</p> <p>14 public health focuses on factors that cause and</p> <p>15 provoke asthma?</p> <p>16 MS. BROWN: Objection to the form of the</p> <p>17 question.</p> <p>18 THE WITNESS: It's a focus.</p> <p>19 BY MS. PARFITT:</p> <p>20 Q Is it fair to say that you have a</p> <p>21 particular interest in air pollutants, and that</p> <p>22 includes secondhand smoke and mouse allergens?</p> <p>23 A I agree with most of what you said, but</p> <p>24 not literally the way you said it, because I don't</p> <p>25 think mouse allergen's a pollutant. So I'm</p>	<p>1 Q Okay. Do you know what the -- do you</p> <p>2 have an understanding of what the allegations are</p> <p>3 against Johnson & Johnson?</p> <p>4 MS. BROWN: Objection to the form.</p> <p>5 THE WITNESS: Which -- which ones?</p> <p>6 BY MS. PARFITT:</p> <p>7 Q Do you know why you're -- Johnson &</p> <p>8 Johnson is being sued?</p> <p>9 MS. BROWN: Objection.</p> <p>10 Counsel, are you asking a legal</p> <p>11 question?</p> <p>12 MS. PARFITT: No.</p> <p>13 BY MS. PARFITT:</p> <p>14 Q Do you have any understanding of the</p> <p>15 allegations or the nature of the lawsuit against</p> <p>16 Johnson & Johnson, the company that's retained you</p> <p>17 to provide expert legal testimony?</p> <p>18 MS. BROWN: Same objection.</p> <p>19 THE WITNESS: I think, generally</p> <p>20 speaking, what I understand is that there's an</p> <p>21 allegation that talcum powder causes ovarian</p> <p>22 cancer.</p> <p>23 BY MS. PARFITT:</p> <p>24 Q Okay. Do you have an understanding of</p> <p>25 the allegations against Imerys?</p>

Gregory B. Diette, M.D.

Page 110	Page 112
<p>1 MS. BROWN: Objection.</p> <p>2 THE WITNESS: I don't have any separate</p> <p>3 understanding.</p> <p>4 BY MS. PARFITT:</p> <p>5 Q Okay. Do you know who Imerys are -- is</p> <p>6 or are?</p> <p>7 A I'm aware that it's a supply company of</p> <p>8 some sort, but I don't know much more about them.</p> <p>9 Q All right. And do you have an</p> <p>10 understanding of the allegations against the</p> <p>11 Personal Care Products Corporation --</p> <p>12 MS. BROWN: Objection.</p> <p>13 BY MS. PARFITT:</p> <p>14 Q -- otherwise known as the PCPC?</p> <p>15 MS. BROWN: Objection. Calls for</p> <p>16 speculation.</p> <p>17 THE WITNESS: I don't --</p> <p>18 MR. LOCKE: Objection.</p> <p>19 BY MS. PARFITT:</p> <p>20 Q You don't.</p> <p>21 A I don't know who that is.</p> <p>22 Q All right. Have you ever seen a</p> <p>23 complaint in this case?</p> <p>24 MS. BROWN: Objection.</p> <p>25 BY MS. PARFITT:</p>	<p>1 through it quickly and just get a sense of what</p> <p>2 the case is about.</p> <p>3 BY MS. PARFITT:</p> <p>4 Q And then what do you do with it?</p> <p>5 MS. BROWN: Form.</p> <p>6 BY MS. PARFITT:</p> <p>7 Q Do you keep it?</p> <p>8 A Oh, not forever. I mean if the case is</p> <p>9 over, then I destroy it with all the other</p> <p>10 materials.</p> <p>11 Q Well, this case is far from over.</p> <p>12 Have -- do you still have --</p> <p>13 MS. BROWN: Counsel, just ask the</p> <p>14 question.</p> <p>15 BY MS. PARFITT:</p> <p>16 Q -- a copy of the complaint?</p> <p>17 MS. MILLER: You asked about a state</p> <p>18 court case.</p> <p>19 MS. PARFITT: No. I said was there --</p> <p>20 hey -- again, hey, ladies, I'm sorry, I think the</p> <p>21 two of you are going to have to agree who is going</p> <p>22 to com- -- who's going to complain -- who's going</p> <p>23 to object. One of you can object.</p> <p>24 MS. BROWN: Well, if you're going to</p> <p>25 complain, I'm going to object.</p>
Page 111	Page 113
<p>1 Q And when I say "this case," I'm talking</p> <p>2 about this case of talcum powder products and</p> <p>3 ovarian cancer, be it in an MDL context or a state</p> <p>4 context.</p> <p>5 MS. BROWN: Same objection.</p> <p>6 MS. MILLER: With any complaint, any</p> <p>7 talcum --</p> <p>8 MS. PARFITT: Any -- yeah, has he ever</p> <p>9 seen a complaint in any talcum powder product and</p> <p>10 ovarian cancer case.</p> <p>11 MS. BROWN: Objection to the form.</p> <p>12 THE WITNESS: I'm sure I must have.</p> <p>13 BY MS. PARFITT:</p> <p>14 Q You're sure you must have.</p> <p>15 Is it in the materials that you have</p> <p>16 reviewed for purposes of your -- your deposition</p> <p>17 today or for purposes of the report you prepared?</p> <p>18 A No.</p> <p>19 MS. BROWN: Objection.</p> <p>20 BY MS. PARFITT:</p> <p>21 Q Okay. If you have seen it, what have</p> <p>22 you done with it?</p> <p>23 MS. BROWN: Objection. Vague.</p> <p>24 THE WITNESS: Well, the same thing I do</p> <p>25 with any complaint, which is just to try to read</p>	<p>1 MS. PARFITT: Okay.</p> <p>2 MS. BROWN: Please just ask the</p> <p>3 question. No speeches.</p> <p>4 MS. PARFITT: Then, please, and I --</p> <p>5 listen, I think that we're getting at a crossroads</p> <p>6 here. One person gets to object. And let me</p> <p>7 remind you what the CMO says, because I know you</p> <p>8 know that --</p> <p>9 MS. BROWN: Counsel --</p> <p>10 MS. PARFITT: And I'm not admonishing.</p> <p>11 Let me finish, Counsel --</p> <p>12 MS. BROWN: Don't yell at me.</p> <p>13 MS. PARFITT: -- and then you can speak.</p> <p>14 MS. BROWN: You're raising your tone at</p> <p>15 me.</p> <p>16 MS. PARFITT: Well, the camera will --</p> <p>17 oh, please, don't be so condescending.</p> <p>18 MS. BROWN: Sure, it's going to reflect</p> <p>19 that you're raising your tone.</p> <p>20 MS. PARFITT: I hope -- I hope that the</p> <p>21 Judge sees this because we're probably --</p> <p>22 MS. BROWN: We are well aware of the</p> <p>23 CMO.</p> <p>24 MS. PARFITT: -- going to have to call</p> <p>25 him soon.</p>

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 114</p> <p>1 MS. BROWN: We are complying with it. 2 We're happy to call the Judge. 3 MS. PARFITT: So the CMO says that you 4 get to say, "Objection. Form." That's what you 5 get to say. 6 You have a wonderful opportunity at the 7 end of this deposition to ask him as many 8 questions as you like, but for right now, my time, 9 my deposition. It's, "Objection. Form." And I 10 really would appreciate that courtesy. I will 11 give it to you, but I would appreciate getting it 12 back. So -- 13 MS. BROWN: And to be clear -- 14 MS. PARFITT: No, Counsel, no more 15 speeches. No more speeches. 16 MS. BROWN: You just made a speech, and 17 I'm going to respond -- 18 MS. PARFITT: No more speeches, Counsel. 19 My deposition. 20 MS. BROWN: No, Counsel. 21 MS. PARFITT: Not your deposition. 22 BY MS. PARFITT: 23 Q Next question I have -- 24 MS. PARFITT: No more questions, 25 Counsel. You want me to depose you?</p>	<p style="text-align: right;">Page 116</p> <p>1 THE WITNESS: Can you say it again? 2 BY MS. PARFITT: 3 Q Sure. 4 A Yeah. 5 Q Have you ever been provided 6 gynecological care or treatment for a woman who 7 has been diagnosed with ovarian cancer? 8 A So there's just a couple of things 9 there, and I think maybe I heard it wrong. 10 Did you say been provided care? 11 Q Have you ever provided -- 12 A Provided. Okay. I'm sorry. I thought 13 you said "been provided." 14 Q No, no, no, no. 15 MS. MILLER: You did say that. 16 THE WITNESS: I thought it sounded like 17 did I get care. I was like -- 18 MS. MILLER: You did -- 19 BY MS. PARFITT: 20 Q No, I -- I don't think you did. 21 A Yeah, right. 22 Q I know, that would have been a very 23 awkward question, wouldn't it? 24 Have you ever provided gynecological 25 care or treatment for a woman who has been</p>
<p style="text-align: right;">Page 115</p> <p>1 MS. BROWN: Counsel, no. You are 2 raising your tone. 3 MS. PARFITT: Counsel -- 4 MS. BROWN: You are yelling at me. 5 MS. PARFITT: -- you know what, I was 6 told a little bit earlier nobody could hear me. 7 So I have lifted my voice, and now I'm using my 8 stage voice. So now everyone can hear me, and now 9 I'm speaking too loud to you. 10 So I'm going to try -- you know, you 11 can't have it both ways. One speaker, one 12 objectioner. Next question. 13 MS. BROWN: The record will reflect that 14 you are making incessant speeches. Please -- 15 BY MS. PARFITT: 16 Q Are you an oncologist, Dr. Diette? 17 A I am not an oncologist. 18 Q Are you a radiation oncologist? 19 A No. 20 Q Are you a gynecologist? 21 A No. 22 Q Okay. Have you ever provided 23 gynecological care or treatment for a woman who 24 has been diagnosed with ovarian cancer? 25 MS. BROWN: Objection. Form.</p>	<p style="text-align: right;">Page 117</p> <p>1 diagnosed with ovarian cancer? 2 A Sure. And I think it goes back to some 3 of the things I said before where I see people in 4 the hospital who have ovarian cancer, and through 5 my training, you know, for medical school and 6 residency, that was part of our training also, 7 which was to rotate on services where people 8 had every -- every imaginable illness. 9 Q Okay. Well, your residency was how long 10 ago? 11 MS. BROWN: Objection. 12 THE WITNESS: My residency was 1990 to 13 1993. 14 BY MS. PARFITT: 15 Q Okay. So I'm not talking about what you 16 did in 1993, back in that period of time. 17 What I'm talking about is whether or not 18 you have actually provided gynecological care to a 19 woman who presented to you with ovarian cancer? 20 MS. BROWN: Objection to the form. 21 Asked and answered five times. 22 You can answer, Dr. Diette. 23 BY MS. PARFITT: 24 Q And by that, primary care. Not in a 25 consulting role but primary care.</p>

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 118</p> <p>1 MS. BROWN: Same objection.</p> <p>2 THE WITNESS: I think I know your</p> <p>3 question, but could you be specific like --</p> <p>4 BY MS. PARFITT:</p> <p>5 Q Sure.</p> <p>6 A -- like just an example, and then I'll</p> <p>7 know that we're talking about the same thing.</p> <p>8 Q Okay. Have you ever provided primary</p> <p>9 care, gynecological care or treatment for a woman</p> <p>10 who has been diagnosed with ovarian cancer?</p> <p>11 A So --</p> <p>12 MR. LOCKE: Objection.</p> <p>13 THE WITNESS: -- I'm not trying to</p> <p>14 criticize the question, but primary care sounds</p> <p>15 like something that a -- like a family</p> <p>16 practitioner or an internist would do. I think</p> <p>17 you mean something else, so --</p> <p>18 BY MS. PARFITT:</p> <p>19 Q I do. Okay. What I'm talking about is</p> <p>20 if I called up Johns Hopkins and said, I have been</p> <p>21 diagnosed with ovarian cancer, I need to see a</p> <p>22 physician, would I be referred to the pulmonology</p> <p>23 department, your department, or would I be</p> <p>24 referred to a different department?</p> <p>25 MS. BROWN: Objection to the form.</p>	<p style="text-align: right;">Page 120</p> <p>1 hygienist?</p> <p>2 A No.</p> <p>3 Q Okay. Are you what's referred to as a</p> <p>4 mineralogist or a mineral scientist specialist?</p> <p>5 A Neither one.</p> <p>6 Q Are you a geologist?</p> <p>7 A No.</p> <p>8 Q Okay. Is it fair to say that you do not</p> <p>9 hold yourself out in the scientific and medical</p> <p>10 community as an expert with regard to testing</p> <p>11 standards of particulate matter, toxins or</p> <p>12 carcinogens?</p> <p>13 A I think that sounds right.</p> <p>14 Q And that would include testing of</p> <p>15 minerals -- or, excuse me, that would include</p> <p>16 testing of asbestos?</p> <p>17 MS. BROWN: Objection to the form.</p> <p>18 THE WITNESS: Correct.</p> <p>19 BY MS. PARFITT:</p> <p>20 Q And that would include testing of talcum</p> <p>21 powder products?</p> <p>22 A That I -- I don't do that, is that</p> <p>23 right?</p> <p>24 Q Right.</p> <p>25 A Yeah, that's correct.</p>
<p style="text-align: right;">Page 119</p> <p>1 THE WITNESS: Different department,</p> <p>2 assuming it's literally for the care of the</p> <p>3 ovarian cancer.</p> <p>4 BY MS. PARFITT:</p> <p>5 Q Okay. Fair. Thank you.</p> <p>6 Have you ever researched the life</p> <p>7 expectancy of a woman who has ovarian cancer?</p> <p>8 A No.</p> <p>9 MS. BROWN: Objection to the form.</p> <p>10 BY MS. PARFITT:</p> <p>11 Q Are you a pathologist?</p> <p>12 A I am not.</p> <p>13 Q All right. And are you a radiologist?</p> <p>14 A I am not.</p> <p>15 Q Okay. Are you a mineralogist?</p> <p>16 A No.</p> <p>17 Q Are you a toxicologist?</p> <p>18 A No.</p> <p>19 Q Are you a pharmacologist?</p> <p>20 A No.</p> <p>21 Q Okay. Are you a regulatory expert?</p> <p>22 A I don't know what that means, but I</p> <p>23 don't -- I don't use those words to describe</p> <p>24 myself.</p> <p>25 Q Okay. Are you a certified industrial</p>	<p style="text-align: right;">Page 121</p> <p>1 Q All right. Let's talk a little bit</p> <p>2 about your publications and your research.</p> <p>3 Let me direct your attention to -- I</p> <p>4 believe this is Appendix C of your CV, which I</p> <p>5 believe is Exhibit 7.</p> <p>6 Do you have that in front of you?</p> <p>7 A I do.</p> <p>8 Q Okay. I understand, now that I have a</p> <p>9 CV that's dated June of 2017, and the CV I have,</p> <p>10 it says that you've published approximately 167</p> <p>11 publications in peer-reviewed literature.</p> <p>12 Is that correct or incorrect?</p> <p>13 A It was probably true as of June 2017.</p> <p>14 Q All right. So sitting here today in</p> <p>15 April of 2019, approximately how many publications</p> <p>16 in peer-reviewed journals have you published?</p> <p>17 A I think if you look on PubMed, you will</p> <p>18 see more than 200.</p> <p>19 Q Okay. Is it fair to say that you've</p> <p>20 published no papers or studies in the peer-</p> <p>21 reviewed literature about asbestos or asbestos-</p> <p>22 related diseases?</p> <p>23 A Correct.</p> <p>24 Well, can you ask that as two different</p> <p>25 questions?</p>

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 122</p> <p>1 Q Sure.</p> <p>2 A I can help you just clarify what I --</p> <p>3 what I'm trying to answer.</p> <p>4 Q Please.</p> <p>5 A So nothing about asbestos, but if you --</p> <p>6 if you consider asbestos-related diseases to</p> <p>7 include lung cancer, for example, that there are</p> <p>8 publications that bear on lung cancer, and there's</p> <p>9 at least one article, maybe more, on interstitial</p> <p>10 lung diseases, and asbestosis would be an</p> <p>11 interstitial lung disease.</p> <p>12 Q Okay. Can you tell me what those</p> <p>13 articles are?</p> <p>14 A Let's see. Would the -- how do you want</p> <p>15 me to do it, like the number?</p> <p>16 Q If you give me the number, that would be</p> <p>17 fine.</p> <p>18 A Yeah. So number 5 has to do with lung</p> <p>19 cancer.</p> <p>20 Q Now, does that have to do with lung</p> <p>21 cancer and asbestos exposure?</p> <p>22 A No, not specifically.</p> <p>23 Q All right. So that has -- that is not</p> <p>24 lung cancer and asbestos.</p> <p>25 All right. Is there another one?</p>	<p style="text-align: right;">Page 124</p> <p>1 THE WITNESS: So that's a different</p> <p>2 question. So the answer to that is no.</p> <p>3 BY MS. PARFITT:</p> <p>4 Q All right. Have you published any</p> <p>5 papers in the peer-reviewed literature on</p> <p>6 mesothelioma?</p> <p>7 A No.</p> <p>8 Q All right. So nowhere in the 200</p> <p>9 publications that you have prepared would I see</p> <p>10 the word "mesothelioma"?</p> <p>11 A I can't promise that you won't see that</p> <p>12 word in some paper, but there's not a paper whose</p> <p>13 primary topic is about mesothelioma.</p> <p>14 Q All right. Very good.</p> <p>15 Having reviewed your 200 or so</p> <p>16 publications, is it fair to say that there are no</p> <p>17 peer-reviewed publications regarding the subject</p> <p>18 matter of ovarian cancer?</p> <p>19 A That's correct.</p> <p>20 Q Is it fair to say that none of your</p> <p>21 peer-reviewed papers address a diagnosis of</p> <p>22 ovarian cancer?</p> <p>23 MS. BROWN: Objection. Form. I don't</p> <p>24 understand that.</p> <p>25 THE WITNESS: Well, I think -- I think</p>
<p style="text-align: right;">Page 123</p> <p>1 A Yeah, so if you look at number 6, this</p> <p>2 is, you know, a study about evaluating lung masses</p> <p>3 and large lymph nodes.</p> <p>4 Q Yes.</p> <p>5 A So that would include, you know, lung</p> <p>6 cancer in that as well.</p> <p>7 Q Does that include asbestos and lung</p> <p>8 cancer?</p> <p>9 A Not specifically.</p> <p>10 Q All right. Any others?</p> <p>11 A I would say any of the ones where you</p> <p>12 see the word "bronchoscopy," it has something to</p> <p>13 do with lung cancer for the most part, though not</p> <p>14 literally lung cancer and asbestos.</p> <p>15 So, for example, like 21, number 2,</p> <p>16 number 3, you know, all sort of have some bearing</p> <p>17 on at least the -- you know, the care or</p> <p>18 management of people with suspected lung cancer or</p> <p>19 who actually have lung cancer.</p> <p>20 Q Dr. Diette, my question is very specific</p> <p>21 to publications in the peer-reviewed journal that</p> <p>22 deal with the topic of asbestos or asbestos-</p> <p>23 related diseases like lung cancer where the word</p> <p>24 "asbestos" appears in your publication.</p> <p>25 MS. BROWN: Objection to the form.</p>	<p style="text-align: right;">Page 125</p> <p>1 the answer to the one before encompasses, you</p> <p>2 know, something else with the word "ovarian</p> <p>3 cancer" in the question.</p> <p>4 BY MS. PARFITT:</p> <p>5 Q Okay. All right. Have you published</p> <p>6 any peer-reviewed publications that talk about the</p> <p>7 causes of ovarian cancer?</p> <p>8 MS. BROWN: Objection.</p> <p>9 THE WITNESS: No.</p> <p>10 BY MS. PARFITT:</p> <p>11 Q Have you published any peer-reviewed</p> <p>12 papers that talk about risk factors for ovarian</p> <p>13 cancer?</p> <p>14 MS. BROWN: Same objection.</p> <p>15 THE WITNESS: No.</p> <p>16 BY MS. PARFITT:</p> <p>17 Q Have you published any publications in</p> <p>18 the peer-reviewed journal on risk factors for</p> <p>19 mesothelioma?</p> <p>20 A No.</p> <p>21 Q What causes mesothelioma?</p> <p>22 A A few things. You know, asbestos in</p> <p>23 sufficient dose can do it. Radiation can do it.</p> <p>24 There's some other minerals that aren't asbestos</p> <p>25 that are suspected to do it. It can arise on its</p>

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 126</p> <p>1 own spontaneously. And, you know, there's</p> <p>2 thoughts of, at least in the peritoneum, about</p> <p>3 certain kinds of chronic inflammation that may</p> <p>4 lead to that as well.</p> <p>5 Q Okay. Can asbestos cause lung cancer?</p> <p>6 A Yes. In a sufficient dose.</p> <p>7 Q Okay. Is it fair to say that you have</p> <p>8 not published in the peer-reviewed literature any</p> <p>9 studies on talcum powder products as a causative</p> <p>10 factor for ovarian cancer?</p> <p>11 A That is correct.</p> <p>12 Q Is it fair to say that you have not</p> <p>13 published in the peer-reviewed journal any studies</p> <p>14 with regard to talcum powder products as a risk</p> <p>15 factor for ovarian cancer?</p> <p>16 A That's correct.</p> <p>17 Q Is it fair to say to say that there are</p> <p>18 no publications in your peer-reviewed literature</p> <p>19 on the subject of talcum -- of talc as a source of</p> <p>20 asbestos fibers?</p> <p>21 MS. BROWN: Objection. Counsel, I think</p> <p>22 you just misspoke. Do you mean on his CV?</p> <p>23 MS. PARFITT: I'm sorry? I did.</p> <p>24 BY MS. PARFITT:</p> <p>25 Q Is it fair to say --</p>	<p style="text-align: right;">Page 128</p> <p>1 A Right, are there -- no.</p> <p>2 Q Okay. I noted in your CV or in some of</p> <p>3 the readings that you are currently involved in</p> <p>4 some clinical trials.</p> <p>5 Did I -- did I get that correct?</p> <p>6 A I have been involved in trials.</p> <p>7 Q Something recent?</p> <p>8 A Oh, all the time.</p> <p>9 Q Okay. Are you currently involved in any</p> <p>10 clinical trial --</p> <p>11 A Yeah.</p> <p>12 Q -- trials?</p> <p>13 Okay. Do any of them deal with the</p> <p>14 subject of asbestos?</p> <p>15 A No.</p> <p>16 Q Do any of your trials or research deal</p> <p>17 with the subject of talcum powder products?</p> <p>18 A No.</p> <p>19 Q All right. Do you currently have</p> <p>20 ongoing any research work in the area of asbestos?</p> <p>21 MS. BROWN: Objection to the form.</p> <p>22 THE WITNESS: No.</p> <p>23 BY MS. PARFITT:</p> <p>24 Q Do you currently have ongoing in any of</p> <p>25 your research work on the topic of mesothelioma?</p>
<p style="text-align: right;">Page 127</p> <p>1 MS. PARFITT: Thank you.</p> <p>2 BY MS. PARFITT:</p> <p>3 Q Is it fair to say that there are no</p> <p>4 peer-reviewed publications in your CV that discuss</p> <p>5 the subject as -- of talc as a source of asbestos</p> <p>6 fibers?</p> <p>7 A Correct.</p> <p>8 Q Is it fair to say there are no</p> <p>9 publications in a peer-reviewed journal contained</p> <p>10 in your curriculum vitae regarding the association</p> <p>11 or relationship between talcum powder products and</p> <p>12 ovarian cancer?</p> <p>13 MS. BROWN: Objection to the form of the</p> <p>14 question.</p> <p>15 THE WITNESS: Correct.</p> <p>16 BY MS. PARFITT:</p> <p>17 Q Are there any publications in --</p> <p>18 peer-reviewed publications on your curriculum</p> <p>19 vitae regarding the association or relationship</p> <p>20 between asbestos and ovarian cancer?</p> <p>21 MS. BROWN: Objection. Asked and</p> <p>22 answered.</p> <p>23 THE WITNESS: You said are there any --</p> <p>24 BY MS. PARFITT:</p> <p>25 Q Asbestos.</p>	<p style="text-align: right;">Page 129</p> <p>1 A No.</p> <p>2 Q Do you currently have any research work</p> <p>3 ongoing on the topic of talcum powder products?</p> <p>4 A No.</p> <p>5 Q Do you currently have any research in</p> <p>6 the works with regard to work on -- work on</p> <p>7 ovarian cancer?</p> <p>8 A No.</p> <p>9 MS. BROWN: Objection to the form.</p> <p>10 BY MS. PARFITT:</p> <p>11 Q Okay. Would it be fair to say that the</p> <p>12 only report that you have prepared on the topic of</p> <p>13 talcum powder products and ovarian cancer would be</p> <p>14 your litigation report --</p> <p>15 MS. BROWN: Object --</p> <p>16 BY MS. PARFITT:</p> <p>17 Q -- in the multidistrict litigation?</p> <p>18 MS. BROWN: Objection to the form,</p> <p>19 misstates his testimony.</p> <p>20 THE WITNESS: I doubt it's the only</p> <p>21 report. But I certainly did prepare a report for</p> <p>22 this.</p> <p>23 BY MS. PARFITT:</p> <p>24 Q Okay. How many reports have you</p> <p>25 prepared on the issue of talcum powder products</p>

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 130</p> <p>1 and ovarian cancer?</p> <p>2 MS. BROWN: Objection to the form.</p> <p>3 Litigation?</p> <p>4 MS. PARFITT: Litigation reports.</p> <p>5 THE WITNESS: Like less than ten, and --</p> <p>6 and I may be getting the terminology wrong. I</p> <p>7 think there's like a couple of affidavits that I</p> <p>8 think to me are like a report. So I don't know --</p> <p>9 BY MS. PARFITT:</p> <p>10 Q That's a good clarification.</p> <p>11 MS. BROWN: Well, let him finish. Let</p> <p>12 him finish.</p> <p>13 BY MS. PARFITT:</p> <p>14 Q I was trying to clarify for you, Doctor.</p> <p>15 MS. BROWN: Right, but just let him</p> <p>16 finish and then you can clarify.</p> <p>17 MS. PARFITT: Counsel, I will. Please.</p> <p>18 THE WITNESS: But -- but that's what I</p> <p>19 meant, so there's -- there's other things that</p> <p>20 I've sort of written in the litigation work that</p> <p>21 are other than just this report that we're looking</p> <p>22 at here today.</p> <p>23 BY MS. PARFITT:</p> <p>24 Q Okay. So your understanding of what you</p> <p>25 have prepared in written form on talcum powder</p>	<p style="text-align: right;">Page 132</p> <p>1 BY MS. PARFITT:</p> <p>2 Q Okay. So the record is clear and I'm</p> <p>3 clear --</p> <p>4 A Yeah.</p> <p>5 Q -- the only report that you have</p> <p>6 prepared dealing with the -- your evaluation of</p> <p>7 the epidemiology on talcum powder products and</p> <p>8 ovarian cancer is the report that we have marked</p> <p>9 as exhibit -- I guess we haven't had it marked</p> <p>10 yet, but is the report that you filed in this</p> <p>11 case; is that right?</p> <p>12 MS. BROWN: Objection. Misstates his</p> <p>13 testimony.</p> <p>14 MS. MILLER: When you say "report," do</p> <p>15 you mean depositions?</p> <p>16 MS. PARFITT: Counsel, I -- I know --</p> <p>17 we'll get to it. You'll get a -- you'll get a</p> <p>18 question.</p> <p>19 MS. MILLER: It's not about us having a</p> <p>20 question. It's about you asking fair questions.</p> <p>21 MR. TISI: Well, it's not -- her job --</p> <p>22 I'm going to jump in here because --</p> <p>23 MS. PARFITT: Okay. Right.</p> <p>24 MR. TISI: -- now you're double teaming.</p> <p>25 I assume you have competent counsel defending this</p>
<p style="text-align: right;">Page 131</p> <p>1 products and ovarian cancer would be, one,</p> <p>2 affidavits. Correct?</p> <p>3 A Correct.</p> <p>4 Q And two, a legal expert report or more?</p> <p>5 MS. BROWN: Form.</p> <p>6 THE WITNESS: Correct.</p> <p>7 BY MS. PARFITT:</p> <p>8 Q Okay. Do you know whether or not you</p> <p>9 have prepared any legal expert reports like the</p> <p>10 one you prepared here in the MDL?</p> <p>11 MS. BROWN: Objection to the form.</p> <p>12 THE WITNESS: Well, on any topic?</p> <p>13 BY MS. PARFITT:</p> <p>14 Q Affidavits -- no, on ovarian cancer and</p> <p>15 talcum powder products.</p> <p>16 A I don't think I --</p> <p>17 MS. BROWN: I object.</p> <p>18 THE WITNESS: I'm sorry.</p> <p>19 Yeah, I don't know if I've completed</p> <p>20 another -- another report, although I'm just</p> <p>21 trying to think if there was like -- like a case-</p> <p>22 specific report that might have had something in</p> <p>23 it. I mean not a report like this one, meaning</p> <p>24 where -- where the whole topic is just about</p> <p>25 the -- the epidemiology and so forth.</p>	<p style="text-align: right;">Page 133</p> <p>1 deposition. Honestly, you did this last week, and</p> <p>2 you've done it in every deposition, and you in</p> <p>3 particular, and you have a real problem with</p> <p>4 obstructing depositions. You need to stop.</p> <p>5 BY MS. PARFITT:</p> <p>6 Q Okay. Dr. Diette, I'll try and break it</p> <p>7 down, and I'm just trying to -- this isn't a trick</p> <p>8 question. So you let me know if you don't</p> <p>9 understand my question.</p> <p>10 MS. BROWN: And, Counsel, in all</p> <p>11 seriousness, in an effort to help, are you meaning</p> <p>12 to include or exclude the Ingham affidavit, which</p> <p>13 I think is the --</p> <p>14 MS. PARFITT: I haven't gotten to it. I</p> <p>15 really haven't gotten to it. That's -- that's --</p> <p>16 I'm hoping that the doctor knows what he -- what</p> <p>17 he's filed.</p> <p>18 Let's have marked as Plaintiffs' Exhibit</p> <p>19 No. 10.</p> <p>20 (Diette Exhibit No. 10 was marked</p> <p>21 for identification.)</p> <p>22 BY MS. PARFITT:</p> <p>23 Q Okay. Dr. Diette, let me present you</p> <p>24 with an "Expert Report of Gregory Diette for</p> <p>25 General Causation Daubert Hearing." Okay.</p>

Gregory B. Diette, M.D.

Page 134	Page 136
<p>1 A That's this --</p> <p>2 Q Do you see that?</p> <p>3 A That's this one for here?</p> <p>4 Q Correct.</p> <p>5 A Yes.</p> <p>6 Q All right. Now, you've identified on</p> <p>7 the record that the report I have handed you,</p> <p>8 which is Exhibit No. 10, is a copy of your federal</p> <p>9 court expert report in the matter of -- dealing</p> <p>10 with the issues of talc and ovarian cancer,</p> <p>11 correct?</p> <p>12 A Exactly right.</p> <p>13 Q And in addition to that report, you have</p> <p>14 prepared some affidavits in the past also</p> <p>15 addressing the topic of talcum powder products and</p> <p>16 ovarian cancer, correct?</p> <p>17 A That's correct.</p> <p>18 Q Okay. Have you prepared any reports on</p> <p>19 talcum powder products and ovarian cancer outside</p> <p>20 of the legal context?</p> <p>21 MS. BROWN: Objection to the form.</p> <p>22 THE WITNESS: No.</p> <p>23 BY MS. PARFITT:</p> <p>24 Q Okay. And have you provided any other</p> <p>25 type of written report in a legal context, aside</p>	<p>1 BY MS. PARFITT:</p> <p>2 Q That's correct.</p> <p>3 A Oh, yeah, so then, no, nothing --</p> <p>4 nothing for which I've been disclosed.</p> <p>5 Q Okay. But I take it that you have been</p> <p>6 retained -- you're currently retained to work on</p> <p>7 some other cases other than talcum powder products</p> <p>8 and ovarian cancer, is that correct, by Johnson &</p> <p>9 Johnson?</p> <p>10 MS. BROWN: Counsel, I'm going to -- to</p> <p>11 the extent you're asking about consulting</p> <p>12 engagements, I'm going to instruct him not to</p> <p>13 answer.</p> <p>14 BY MS. PARFITT:</p> <p>15 Q No, I'm asking this: Are you an expert</p> <p>16 on behalf of Johnson & Johnson and asbestos and --</p> <p>17 and ovarian cancer cases?</p> <p>18 A So there's a subtlety there, right,</p> <p>19 because -- I mean you may call this an asbestos</p> <p>20 and ovarian cancer case. I think it's a talcum</p> <p>21 powder and ovarian cancer case.</p> <p>22 Q Okay.</p> <p>23 A There's nothing that's about asbestos</p> <p>24 separately from what we're talking about here.</p> <p>25 Q Fair enough. Have you been retained by</p>
Page 135	Page 137
<p>1 from affidavits and the MDL report that you have</p> <p>2 in front of you?</p> <p>3 MS. BROWN: Form.</p> <p>4 BY MS. PARFITT:</p> <p>5 Q On talcum powder products and ovarian</p> <p>6 cancer. I'm just trying to find out your world.</p> <p>7 A No, I understand. And I'm not sure if</p> <p>8 there could be like a work in progress. But</p> <p>9 you're talking about completed, completed like</p> <p>10 products like this, right?</p> <p>11 Q Correct.</p> <p>12 A I -- I can't think of another one.</p> <p>13 Q Okay. Do you have another report and/or</p> <p>14 affidavit in progress in the talcum powder</p> <p>15 products cases and ovarian cancer?</p> <p>16 MS. BROWN: Dr. Diette, I'm going to</p> <p>17 instruct you to the extent you're doing any work</p> <p>18 on this issue that is in a consulting nature and</p> <p>19 has not been disclosed, you should not disclose</p> <p>20 that here.</p> <p>21 I assume counsel is only asking for</p> <p>22 situations in which you have been disclosed as an</p> <p>23 expert, and with that, you can answer the</p> <p>24 question.</p> <p>25 THE WITNESS: Is that right?</p>	<p>1 Johnson & Johnson to testify as a legal expert in</p> <p>2 any talcum powder product cases and meso- --</p> <p>3 mesothelioma?</p> <p>4 A Yes.</p> <p>5 Q Okay. Are you currently an expert in</p> <p>6 any of those cases?</p> <p>7 A Yes.</p> <p>8 Q How many?</p> <p>9 MS. BROWN: And again, Doctor, to the</p> <p>10 extent you've been disclosed, you can answer the</p> <p>11 question.</p> <p>12 THE WITNESS: So I don't -- I don't know</p> <p>13 the count then. I would estimate ten, but I could</p> <p>14 be off by a couple.</p> <p>15 BY MS. PARFITT:</p> <p>16 Q Have you given depositions in those</p> <p>17 cases yet?</p> <p>18 A In some cases I have.</p> <p>19 Q Okay. Is this the first deposition that</p> <p>20 you have given in talcum powder products and</p> <p>21 ovarian cancer?</p> <p>22 MS. BROWN: Objection.</p> <p>23 THE WITNESS: I don't think so.</p> <p>24 BY MS. PARFITT:</p> <p>25 Q Okay. Did you give testimony in the</p>

35 (Pages 134 to 137)

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 138</p> <p>1 Ingham case?</p> <p>2 A I did.</p> <p>3 Q Okay. Did you testify at trial at the</p> <p>4 Ingham case?</p> <p>5 A I did not.</p> <p>6 Q Okay. Is there any other case other</p> <p>7 than the Ingham case where you have given</p> <p>8 deposition in an ovarian cancer and a talcum</p> <p>9 powder case?</p> <p>10 A I think there's at least one other one.</p> <p>11 Q Okay. Do you remember the name of it?</p> <p>12 A I don't. I could look at my testimony</p> <p>13 list and see if I can figure it out.</p> <p>14 Q Okay. And we'll have that marked as</p> <p>15 well. Why don't we have that marked as Diette</p> <p>16 Exhibit -- it's part of your exhibit number --</p> <p>17 it's part of your report, but we'll have it marked</p> <p>18 as a separate exhibit.</p> <p>19 (Counsel conferring.)</p> <p>20 BY MS. PARFITT:</p> <p>21 Q Let me show you what's -- we'll have</p> <p>22 marked as Exhibit No. 11.</p> <p>23 (Diette Exhibit No. 11 was marked</p> <p>24 for identification.)</p> <p>25 BY MS. PARFITT:</p>	<p style="text-align: right;">Page 140</p> <p>1 yes.</p> <p>2 Q Okay. The last date I have here is</p> <p>3 September 28, '18.</p> <p>4 A No. It should go further.</p> <p>5 MS. BROWN: We have another page,</p> <p>6 Counsel.</p> <p>7 MS. PARFITT: Okay.</p> <p>8 THE WITNESS: I think it's two-sided, so</p> <p>9 it's the back of that page.</p> <p>10 MS. PARFITT: Okay. Well --</p> <p>11 MS. BROWN: Do you want my copy?</p> <p>12 MS. PARFITT: That would be great. I</p> <p>13 appreciate that. I will give it right back to</p> <p>14 you.</p> <p>15 BY MS. PARFITT:</p> <p>16 Q Okay. All right. So the last date is</p> <p>17 February 22nd, 2019; is that correct?</p> <p>18 A That is.</p> <p>19 Q All right. Are you able to circle for</p> <p>20 me which cases are cases in which you have been</p> <p>21 retained as an expert in the -- on the topic of</p> <p>22 talcum powder products and ovarian cancer?</p> <p>23 MS. BROWN: Objection to the form.</p> <p>24 You can answer to the extent you know,</p> <p>25 Doctor.</p>
<p style="text-align: right;">Page 139</p> <p>1 Q All right. Let me show you what's</p> <p>2 Exhibit 11.</p> <p>3 MS. PARFITT: We have a copy for</p> <p>4 counsel.</p> <p>5 MS. BROWN: Thank you.</p> <p>6 MR. ROSEN: I think there's --</p> <p>7 THE WITNESS: Oh, there's two.</p> <p>8 MS. PARFITT: Oh, okay, we'll take one</p> <p>9 back. Thank you. Okay. Very good.</p> <p>10 BY MS. PARFITT:</p> <p>11 Q Dr. Diette, does this represent an</p> <p>12 accurate list of cases in which you have been</p> <p>13 retained as an expert since I believe 2014?</p> <p>14 A It is.</p> <p>15 Q All right. Are there any additions to</p> <p>16 this list of cases --</p> <p>17 A I'm sorry.</p> <p>18 Q -- where you've given testimony?</p> <p>19 A I'm sorry. I think I -- I wasn't paying</p> <p>20 attention to your last question.</p> <p>21 Q That's all right.</p> <p>22 A Did you say is this a list of cases that</p> <p>23 I provided depositions?</p> <p>24 Q Expert testimony.</p> <p>25 A Expert testimony. Then the answer is</p>	<p style="text-align: right;">Page 141</p> <p>1 THE WITNESS: I actually don't. I'd</p> <p>2 have to look it up to figure out if I'm right that</p> <p>3 there is one on here, but I don't know -- and</p> <p>4 other than Ingham, right?</p> <p>5 BY MS. PARFITT:</p> <p>6 Q Yes, sir.</p> <p>7 A Other than Ingham, yeah, so I -- I'm not</p> <p>8 sure. I can't tell.</p> <p>9 Q All right. Have you -- we talked about</p> <p>10 your peer-reviewed publications. Are any of your</p> <p>11 public -- peer-reviewed publications discussing</p> <p>12 cohort studies?</p> <p>13 MS. BROWN: Objection to the form.</p> <p>14 THE WITNESS: So some of them are cohort</p> <p>15 studies.</p> <p>16 BY MS. PARFITT:</p> <p>17 Q But you have performed --</p> <p>18 MS. BROWN: Let him answer, please.</p> <p>19 MS. PARFITT: Sure.</p> <p>20 THE WITNESS: That I performed, yes.</p> <p>21 BY MS. PARFITT:</p> <p>22 Q All right. So in your carrier as a</p> <p>23 medical doctor, you have published cohort studies?</p> <p>24 A I have.</p> <p>25 Q What have been the general topics of</p>

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 142</p> <p>1 those cohort studies?</p> <p>2 A Generally speaking, things related to</p> <p>3 respiratory diseases and -- and things people</p> <p>4 inhale.</p> <p>5 Q All right. Have you published case-</p> <p>6 control studies?</p> <p>7 A I don't know. I can't think of one. It</p> <p>8 doesn't mean that there isn't one, but I'm -- I</p> <p>9 can't think of a case-control study.</p> <p>10 Q All right. Is it fair to say that none</p> <p>11 of the published cohort studies address the issue</p> <p>12 of talcum powder products and ovarian cancer?</p> <p>13 A Correct.</p> <p>14 Q And is it fair to say that none of the</p> <p>15 cohort studies that you published address the</p> <p>16 issue of talcum powder products and mesothelioma?</p> <p>17 A Correct.</p> <p>18 Q Is it fair to say that none of the</p> <p>19 cohort studies that you have published address the</p> <p>20 issue of asbestos and mesothelioma?</p> <p>21 A Correct.</p> <p>22 Q Is it fair to say that -- that the</p> <p>23 majority of your publications in your -- listed in</p> <p>24 your curriculum CV and those that you said you</p> <p>25 have published since 2017 deal primarily in the</p>	<p style="text-align: right;">Page 144</p> <p>1 MS. BROWN: Wait. Hold on. Is that a</p> <p>2 question?</p> <p>3 MS. PARFITT: Mm-hmm.</p> <p>4 MS. BROWN: I didn't understand that.</p> <p>5 If you understood it, you can answer.</p> <p>6 THE WITNESS: Well, the papers I was</p> <p>7 thinking about had to do with methods and</p> <p>8 quality -- quality assessment in terms of</p> <p>9 healthcare.</p> <p>10 BY MS. PARFITT:</p> <p>11 Q Okay.</p> <p>12 A I don't know if I've published anything</p> <p>13 on epi methods, meaning like, you know, the topic</p> <p>14 of a case-control study or --</p> <p>15 Q Right.</p> <p>16 A -- cohort studies, things of that sort.</p> <p>17 Q So it would be fair to say that you have</p> <p>18 not published in a peer-reviewed journal a paper</p> <p>19 on study designs, correct?</p> <p>20 MS. BROWN: Objection to the form.</p> <p>21 THE WITNESS: I would have to look back</p> <p>22 and see. I mean it's -- it's possible I've been</p> <p>23 involved in something that -- that -- I mean it's</p> <p>24 just hard to remember. It's 200 plus papers,</p> <p>25 so --</p>
<p style="text-align: right;">Page 143</p> <p>1 research interests of lung disease, COPD,</p> <p>2 asthma --</p> <p>3 MS. BROWN: Objection --</p> <p>4 BY MS. PARFITT:</p> <p>5 Q -- pulmonary medicine, lung diseases?</p> <p>6 MS. BROWN: Objection to the form.</p> <p>7 THE WITNESS: There's certainly plenty</p> <p>8 there. You know, I get different feedback from</p> <p>9 different people who look at my CV to tell whether</p> <p>10 or not it's, you know, all that or whether there's</p> <p>11 other things. I think people read into it what</p> <p>12 they -- what they see. Because there's -- you</p> <p>13 know, there's ICU research topics, there's</p> <p>14 procedure-related topics, there's radiology</p> <p>15 topics. I mean there's all -- all sorts of</p> <p>16 different things besides those.</p> <p>17 BY MS. PARFITT:</p> <p>18 Q Okay. Do you publish on methods and</p> <p>19 methodology?</p> <p>20 MS. BROWN: Form.</p> <p>21 THE WITNESS: So I think there's a</p> <p>22 couple of methods -- methods related papers.</p> <p>23 BY MS. PARFITT:</p> <p>24 Q Papers that deal primarily with</p> <p>25 epidemiological methodology?</p>	<p style="text-align: right;">Page 145</p> <p>1 BY MS. PARFITT:</p> <p>2 Q Right. So nothing you can remember</p> <p>3 today.</p> <p>4 A Correct.</p> <p>5 Q Okay. And have you published on the</p> <p>6 Bradford Hill factors?</p> <p>7 MS. BROWN: Form.</p> <p>8 MR. LOCKE: Objection.</p> <p>9 THE WITNESS: So I've not written a</p> <p>10 paper about Bradford Hill.</p> <p>11 BY MS. PARFITT:</p> <p>12 Q All right. In any of the 200 papers</p> <p>13 that you have published in a peer-reviewed</p> <p>14 journal, do you set forth in those papers the</p> <p>15 Bradford Hill framework?</p> <p>16 MS. BROWN: Objection to the form of the</p> <p>17 question.</p> <p>18 THE WITNESS: You couldn't do it.</p> <p>19 Right. I mean, it's -- the papers that I write</p> <p>20 are primary research papers, and that framework</p> <p>21 doesn't belong in those papers, but we articulate</p> <p>22 the -- the issues that are -- that are relevant</p> <p>23 for a Bradford Hill analysis.</p> <p>24 BY MS. PARFITT:</p> <p>25 Q Okay. Well, in this expert report that</p>

37 (Pages 142 to 145)

Gregory B. Diette, M.D.

Page 146	Page 148
<p>1 you did file in the federal court, you stated</p> <p>2 specifically that you followed the Bradford Hill</p> <p>3 framework. Do you recall saying that?</p> <p>4 A I -- I do. There was more to it, but it</p> <p>5 included that.</p> <p>6 Q Okay. So what I'm asking you, in any of</p> <p>7 the papers, whether they be cohort study, case</p> <p>8 control, other research and scientific</p> <p>9 publications that you've listed on your curriculum</p> <p>10 vitae, have you stated in those papers that you</p> <p>11 are following or are guided by the Bradford Hill</p> <p>12 framework?</p> <p>13 MS. BROWN: Objection. He just answered</p> <p>14 that.</p> <p>15 THE WITNESS: Yeah, it's sort of baked</p> <p>16 into what we do. So it's like in -- I mean the</p> <p>17 answer is no, generally, but -- but we include</p> <p>18 things in a way that they fit with what Bradford</p> <p>19 Hill considerations are. But there's not one that</p> <p>20 was called like the Bradford Hill approach or</p> <p>21 something.</p> <p>22 BY MS. PARFITT:</p> <p>23 Q Okay. And by --</p> <p>24 MS. BROWN: Let him finish.</p> <p>25 Were you finished, Doctor?</p>	<p>1 different than what you asked? Because I'm</p> <p>2 just --</p> <p>3 BY MS. PARFITT:</p> <p>4 Q It is.</p> <p>5 This would be some original research</p> <p>6 that you might be -- got a funding or a grant or</p> <p>7 something.</p> <p>8 A I see. Nothing like that.</p> <p>9 Q Okay. Have you received any funds --</p> <p>10 any funding or any grants to study mesothelioma?</p> <p>11 A No.</p> <p>12 Q Have you received any funding or grants</p> <p>13 to study asbestos?</p> <p>14 A No.</p> <p>15 Q Have you received any funding or grants</p> <p>16 to study talcum powder products and their</p> <p>17 association with ovarian cancer?</p> <p>18 MS. BROWN: Objection to the form.</p> <p>19 THE WITNESS: No.</p> <p>20 BY MS. PARFITT:</p> <p>21 Q Have you ever published in peer-reviewed</p> <p>22 literature a causation analysis or a review</p> <p>23 article asking whether an exposure causes a</p> <p>24 disease?</p> <p>25 MS. BROWN: Objection to the form of the</p>
Page 147	Page 149
<p>1 THE WITNESS: I'm okay. Thank you.</p> <p>2 MS. PARFITT: Thank you.</p> <p>3 BY MS. PARFITT:</p> <p>4 Q Assume I did a search of the word</p> <p>5 "Bradford Hill" in the 167 papers that you have</p> <p>6 published in the peer-reviewed journal, would it</p> <p>7 surprise you if those words did not appear?</p> <p>8 MS. BROWN: Objection to the form.</p> <p>9 THE WITNESS: It wouldn't surprise me,</p> <p>10 but I -- I don't know that it's not there</p> <p>11 somewhere. And I would search more broadly than</p> <p>12 just those 167. I would look at the more recent</p> <p>13 ones too. I mean I can't say that it's not there,</p> <p>14 but there's not a paper about Bradford Hill.</p> <p>15 BY MS. PARFITT:</p> <p>16 Q Okay. Have you been involved in any</p> <p>17 original research on asbestos in general?</p> <p>18 MS. BROWN: Objection to the form.</p> <p>19 THE WITNESS: I have not.</p> <p>20 BY MS. PARFITT:</p> <p>21 Q Have you -- have you conducted any</p> <p>22 original research on ovarian cancer?</p> <p>23 MS. BROWN: Objection to the form, asked</p> <p>24 and answered.</p> <p>25 THE WITNESS: I guess, I mean -- is it</p>	<p>1 question.</p> <p>2 THE WITNESS: I don't know. I would</p> <p>3 have to look back over. I don't -- like I don't</p> <p>4 know if I would use those words "causation</p> <p>5 analysis," but we certainly write -- did you say</p> <p>6 review article?</p> <p>7 BY MS. PARFITT:</p> <p>8 Q Yes.</p> <p>9 A So I don't write many review articles.</p> <p>10 They're really -- they're really low quality</p> <p>11 academic products for the most part, and so I try</p> <p>12 to focus more on original research.</p> <p>13 Q All right. Well, same question applied</p> <p>14 to original research.</p> <p>15 MS. BROWN: Objection to the form.</p> <p>16 THE WITNESS: Well, it wouldn't be -- I</p> <p>17 mean that wouldn't be an original research</p> <p>18 article.</p> <p>19 BY MS. PARFITT:</p> <p>20 Q Okay. Have you ever performed any</p> <p>21 research on the environmental impacts of talcum</p> <p>22 powder products and ovarian cancer?</p> <p>23 MS. BROWN: Objection to the form,</p> <p>24 vague.</p> <p>25 THE WITNESS: No.</p>

38 (Pages 146 to 149)

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 150</p> <p>1 BY MS. PARFITT:</p> <p>2 Q Environmental impacts of diseases is</p> <p>3 something -- is a topic that you are interesting</p> <p>4 in, correct?</p> <p>5 A I am.</p> <p>6 Q You've studied the impact of</p> <p>7 environmental effects on lung diseases, correct?</p> <p>8 A I have.</p> <p>9 Q In fact, that's something you continue</p> <p>10 to be interested in, correct?</p> <p>11 A I am.</p> <p>12 Q But you've not studied any environmental</p> <p>13 impacts on ovarian cancer, correct?</p> <p>14 A Correct.</p> <p>15 MS. BROWN: Asked and answered.</p> <p>16 BY MS. PARFITT:</p> <p>17 Q Would it be fair to say that prior to</p> <p>18 being retained by Johnson & Johnson sometime in</p> <p>19 2017, you had done no research on the issue of</p> <p>20 talcum powder products and ovarian cancer?</p> <p>21 MS. BROWN: Objection to the form,</p> <p>22 misstates his testimony.</p> <p>23 THE WITNESS: I think it's the same as</p> <p>24 before. Right. I mean you went through each --</p> <p>25 each item, and my answer was no.</p>	<p style="text-align: right;">Page 152</p> <p>1 Q And to give you some -- a reference,</p> <p>2 we'll spend a little time on that before we get</p> <p>3 into your report. All right? Fair?</p> <p>4 A Sounds good.</p> <p>5 Q Okay. What is Medical Science</p> <p>6 Affiliates?</p> <p>7 A I think they -- they call themselves an</p> <p>8 environmental consulting company.</p> <p>9 Q How long have you been involved with</p> <p>10 Medical Science Affiliates?</p> <p>11 MS. BROWN: Form.</p> <p>12 THE WITNESS: So involved, I guess we'll</p> <p>13 have to sort, but I -- I've known about them and</p> <p>14 done some work with them for about ten years.</p> <p>15 BY MS. PARFITT:</p> <p>16 Q Okay. And I too want to sort, so let me</p> <p>17 ask you this: When were you first introduced to</p> <p>18 Medical Science Affiliates?</p> <p>19 A Well, I guess if it's ten years, it</p> <p>20 would have been about ten years ago.</p> <p>21 Q And what were -- how did it come about</p> <p>22 that you learned of a group called Medical Science</p> <p>23 Affiliates?</p> <p>24 A There was a woman who worked there</p> <p>25 then -- I don't remember what her name is, she's</p>
<p style="text-align: right;">Page 151</p> <p>1 BY MS. PARFITT:</p> <p>2 Q So it was not until you were retained by</p> <p>3 Johnson & Johnson that you conducted any research</p> <p>4 on the topic of ovarian cancer and talcum powder</p> <p>5 products, correct?</p> <p>6 MS. BROWN: Objection to the form,</p> <p>7 misstates his testimony.</p> <p>8 THE WITNESS: That is right.</p> <p>9 MS. PARFITT: Okay. And is now a good</p> <p>10 time for a bio break or is it --</p> <p>11 MS. PARFITT: Sure.</p> <p>12 THE WITNESS: If you're in the middle of</p> <p>13 something, I --</p> <p>14 MS. PARFITT: No, no, this is fine.</p> <p>15 We'll just move into another area quickly, yeah.</p> <p>16 THE VIDEOGRAPHER: The time is</p> <p>17 11:14 a m., and we're going off the record.</p> <p>18 (Recess.)</p> <p>19 THE VIDEOGRAPHER: The time is</p> <p>20 11:24 a m., and we are back on the record.</p> <p>21 BY MS. PARFITT:</p> <p>22 Q All right. Dr. Diette, I want to talk</p> <p>23 for a moment about Medical Science Affiliates.</p> <p>24 All right?</p> <p>25 A Okay.</p>	<p style="text-align: right;">Page 153</p> <p>1 not there anymore -- and she knew a colleague of</p> <p>2 mine, and they were I think at the time looking</p> <p>3 for somebody to take on an epidemiology project, a</p> <p>4 review. And so he -- he sent around like a note</p> <p>5 or talked to us, I don't remember how he did it,</p> <p>6 but to see if anybody was interested in -- in</p> <p>7 doing an epidemiology project.</p> <p>8 Q Who was that colleague?</p> <p>9 A I think it was Hank Fessler, but I could</p> <p>10 be wrong. That's a while ago.</p> <p>11 Q And what is his position within the</p> <p>12 university?</p> <p>13 A He works in pulmonary.</p> <p>14 Q Okay. So you were -- you were then</p> <p>15 engaged by Medical Science Affiliates to do an</p> <p>16 epidemiological report for them?</p> <p>17 MS. BROWN: Objection. Misstates</p> <p>18 testimony.</p> <p>19 THE WITNESS: I don't know about</p> <p>20 engaged. I mean my -- my relationship is as an</p> <p>21 independent contractor. So it's like -- it's not</p> <p>22 like I have an agreement to do anything with them</p> <p>23 or for them. But that's -- that's the place</p> <p>24 where, you know, they organize the materials for</p> <p>25 me to look over and to -- and to do the</p>

Gregory B. Diette, M.D.

Page 154	Page 156
<p>1 epidemiological review. 2 BY MS. PARFITT: 3 Q Okay. Your counsel has objected, as you 4 heard, to me obtaining a copy of your agreement, 5 so I'm going to have to ask you a few more 6 questions about this. 7 What is your arrangement with Medical 8 Science Affiliates? Independent contractor? 9 A That's exactly right. 10 MS. BROWN: He just said it. 11 MS. PARFITT: Okay. I understand. You 12 can take your own deposition, Counsel. It's going 13 to show up on the record too, you're rubbing your 14 head. 15 BY MS. PARFITT: 16 Q Medical Science, you have an independent 17 contract relationship, to do what? 18 A I think what it establishes is that I 19 can use their administrative services as kind of 20 like an outside office for me to do work. 21 Q Okay. So that's one role, they're an 22 outside office. You mentioned, though, that they 23 contracted you to also write an epidemiology 24 report. Correct? 25 A It's --</p>	<p>1 Q More 50? 2 A At least 50. 3 Q Okay. And what has been the topic of 4 those reports that you have prepared for Medical 5 Science Affiliates' clients? 6 MS. BROWN: And I'm going to jump in 7 here. To the extent that those projects are 8 governed by confidentiality agreements, I would 9 ask Dr. Diette that you only disclose that which 10 has been disclosed publicly, for example, in court 11 or at a deposition. 12 MS. PARFITT: Please stop coaching the 13 witness. 14 BY MS. PARFITT: 15 Q Can you answer? 16 MS. BROWN: We're trying to protect 17 confidentiality. 18 MS. PARFITT: I get -- 19 MS. BROWN: I'm instructing him on 20 privilege. 21 MS. PARFITT: That's fine. I 22 understood. He can talk now. 23 THE WITNESS: So I would say that most 24 of the work is in the context of what Ms. Brown 25 said, which is that it wasn't for me to share with</p>
Page 155	Page 157
<p>1 MS. BROWN: Objection to the form. 2 THE WITNESS: It's incorrect. 3 BY MS. PARFITT: 4 Q Okay. Straighten it out for me. 5 A Well, they didn't contract me to do 6 anything. They asked if I was interested in doing 7 this epidemiologic project for a client that they 8 knew of. 9 Q Okay. That helps me. 10 So Medical Science Affiliates reached 11 out -- requested that you do an epidemiological 12 report for one of their clients. 13 A Exactly right. 14 Q Okay. Over the course of ten years that 15 you've been affiliated as an independent 16 contractor with Medical Science Affiliates, how 17 many times have you prepared a report for one of 18 Medical Science Affiliates' clients? 19 A I don't know. 20 Q More than ten? 21 A Sure. 22 Q More than a hundred? 23 A A hundred would be pushing it. So 24 something in the tens, I would say. But not ten. 25 I mean something higher up in --</p>	<p>1 other people. 2 BY MS. PARFITT: 3 Q All right. Is J&J a client of Medical 4 Science Affiliates? 5 A I don't know what their relationship is, 6 like I don't know if you would call them a client 7 or not. 8 Q Okay. Does Medical Science Affiliates 9 do some work for Johnson & Johnson? 10 MS. BROWN: Objection. Speculation. 11 THE WITNESS: So I can tell you about 12 what they do for me with regard to Johnson & 13 Johnson. I don't know about anything else. 14 BY MS. PARFITT: 15 Q All right. Tell me what you know. 16 A Well, like, for example, like in the 17 cases that we've discussed that involve Johnson & 18 Johnson, they've provided a service by collecting 19 the materials, right. So, for example, like when 20 you see that list of materials that -- that I 21 provided that I reviewed, they will collect those 22 and -- and organize them for me. 23 If there's a need to have a meeting or a 24 phone call, they'll help to set that up, right, so 25 that -- so, for example, for the deposition today,</p>

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 158</p> <p>1 they were able to help sort my -- through my 2 schedule, you know, with me, and figure out a day 3 or days, I don't remember what we offered, things 4 of that sort. They'll prepare invoices on my 5 behalf. They'll help edit a report. You know, 6 administrative type things. 7 Q Okay. Let's break that down a little 8 bit. 9 Is it your understanding that Medical 10 Science Affiliates bills Johnson & Johnson -- 11 MS. BROWN: Object -- 12 BY MS. PARFITT: 13 Q -- and invoices them for work? 14 MS. BROWN: Objection to the form, calls 15 for speculation. 16 BY MS. PARFITT: 17 Q If you know. 18 A I don't know where the bill goes because 19 I don't know if it goes to the law firm. Like if 20 it matters to you whether it's directly to Johnson 21 & Johnson or -- I mean I can only guess that, you 22 know, the law firm is not going to pay the bill 23 out of their own pocket. They're probably going 24 to then invoice Johnson & Johnson, but I don't 25 know whether the bill goes directly to Johnson &</p>	<p style="text-align: right;">Page 160</p> <p>1 you said, which is that they billed somebody else 2 for the work that they did. 3 BY MS. PARFITT: 4 Q Do you know who that somebody else is? 5 And I want to remind you you're under oath, 6 Dr. Diette. 7 MS. BROWN: What -- 8 THE WITNESS: What's -- 9 MS. BROWN: Whoa, whoa, whoa. I'm 10 objecting to the implication there. Dr. Diette 11 has done nothing but testify truthfully today. 12 MS. PARFITT: Counsel, objection, form. 13 I'm telling you. 14 BY MS. PARFITT: 15 Q Please go on, Dr. Diette. 16 MS. BROWN: No, but what you just said 17 is inappropriate -- 18 MS. PARFITT: It was not -- 19 MS. BROWN: -- and it violates both the 20 federal rules -- 21 MS. PARFITT: -- violative of anything, 22 Counsel. 23 MS. BROWN: -- as well as deposition 24 protocol. He of course is testifying under oath, 25 and if you're suggesting something otherwise,</p>
<p style="text-align: right;">Page 159</p> <p>1 Johnson or whether it goes to the law firm. 2 Q All right. 3 MS. BROWN: And, Doctor, counsel doesn't 4 want you to guess, so just answer the question the 5 best -- 6 BY MS. PARFITT: 7 Q Dr. Diette, if they -- Medical Science 8 Affiliates collects material for you -- as you say 9 they did, correct? 10 A That's correct. 11 Q -- do they bill you or do they bill 12 someone else? 13 MS. BROWN: Objection to the form. 14 THE WITNESS: They bill someone else. 15 BY MS. PARFITT: 16 Q Okay. So when you testified that J&J -- 17 excuse me, when you testified that you had 18 assistance with regard to the preparation of some 19 of the materials that accompany your report, that 20 was work that you contracted with Medical Service 21 Affiliates to do, and they didn't bill you, they 22 billed somebody else, correct? 23 MS. BROWN: Objection to the form. 24 THE WITNESS: I don't know if 25 "contracted" is right, but -- but they did what</p>	<p style="text-align: right;">Page 161</p> <p>1 that's wildly inappropriate. 2 MS. PARFITT: Counsel, let the Court 3 decide if it's -- I think the Court might decide 4 that your objections and your manner today are 5 wildly inappropriate. 6 BY MS. PARFITT: 7 Q So, Dr. Diette, so we can move forward, 8 do you remember the question? 9 A I remember it, but I think I already 10 answered it. It's -- I don't have a better answer 11 than what I gave you before. 12 Q You don't know who Medical Science 13 billed for the services they rendered to you? 14 A Well, let's look at the invoice if we 15 want to. If it's on the top of that, then I 16 might -- 17 Q It's been blacked out, Dr. Diette. 18 A So it's either a law firm or it's 19 Johnson & Johnson. I don't know whether it's one 20 or the other. 21 MS. BROWN: Counsel, you're 22 misrepresenting the documents. It's very clear 23 who they sent the bill to on the face of the 24 invoice, and it has not been redacted for 25 work-product privilege.</p>

Gregory B. Diette, M.D.

Page 162	Page 164
<p>1 BY MS. PARFITT:</p> <p>2 Q What I want to understand, for purpose</p> <p>3 of the expert report you prepared in this</p> <p>4 litigation, I want you to tell me, if you will,</p> <p>5 every service that Medical Science Affiliates</p> <p>6 performed for you.</p> <p>7 A I don't think I can give you a full</p> <p>8 list. I think that the -- go ahead.</p> <p>9 Q No, no, please, go ahead.</p> <p>10 A All right. So I think the category of</p> <p>11 things that I told you about before are the kinds</p> <p>12 of things that they -- that they did in this case.</p> <p>13 I don't know if I mentioned like arranging like a</p> <p>14 phone call. Like if I was going to have a phone</p> <p>15 call, they would arrange that. Help with -- I</p> <p>16 already talked about editing -- editing reports</p> <p>17 and -- I can't think of another service they did,</p> <p>18 but that's what I can think of right now.</p> <p>19 Q Okay. Did Medical Science Affiliates</p> <p>20 research the scientific literature for you in</p> <p>21 preparation for some of the information contained</p> <p>22 in your expert report?</p> <p>23 A I don't -- I don't think they did any of</p> <p>24 that. I mean, they've -- they've done searches in</p> <p>25 the past on other -- other topics, but I don't</p>	<p>1 something else with the papers?</p> <p>2 Q I'll break it down. Did they do a</p> <p>3 literature search for you?</p> <p>4 A Yeah, and that's what I don't remember.</p> <p>5 So I'm just saying that they've done that at my</p> <p>6 request in the past. But not -- not too much. I</p> <p>7 mean it's actually not that helpful, because I --</p> <p>8 I find it easier to do it myself.</p> <p>9 Q Whether it was helpful or not, my</p> <p>10 question is, did Medical Science Affiliates do any</p> <p>11 literature research for you in -- on the topic of</p> <p>12 talcum powder products and ovarian cancer?</p> <p>13 A I can't give you a better answer. I</p> <p>14 mean I -- I think it sounds to me like you keep</p> <p>15 asking the same thing, and it -- my answer is I'm</p> <p>16 not -- I'm not sure. Like they may have gathered</p> <p>17 a couple of papers, I don't remember if they did</p> <p>18 or not. They certainly didn't do the search, like</p> <p>19 I didn't commission anybody to do like -- like the</p> <p>20 search.</p> <p>21 Q Okay. And how would they deliver that</p> <p>22 information to you? Do they e-mail it to you? Do</p> <p>23 they send it to you? What happens?</p> <p>24 A It depends upon how I ask. So it can</p> <p>25 come as a binder, like the binder you have in</p>
Page 163	Page 165
<p>1 think they did any for this.</p> <p>2 Q All right. So it's your testimony that</p> <p>3 in the talcum powder/ovarian cancer case, they did</p> <p>4 not do any research of the peer-reviewed</p> <p>5 literature; is that correct?</p> <p>6 A Well, let me be clear, when you talk</p> <p>7 about talcum powder and ovarian cancer -- because</p> <p>8 I have to think back with each -- you know, each</p> <p>9 case or whatever, but we're talking about this</p> <p>10 particular matter as you're asking these questions</p> <p>11 or --</p> <p>12 Q Well, that's a -- that's a great point.</p> <p>13 You got involved in talcum powder and ovarian</p> <p>14 cancer cases sometime in 2017. That's your</p> <p>15 testimony.</p> <p>16 A It is.</p> <p>17 Q All right. So at that point in time</p> <p>18 when you became engaged to work on talcum powder</p> <p>19 products and ovarian cancer, what I'm interested</p> <p>20 in knowing is whether or not, whether it was for</p> <p>21 this report, another report, has Medical Science</p> <p>22 Affiliates done any research work of the</p> <p>23 literature on this topic?</p> <p>24 A And by "research work," does that -- do</p> <p>25 you mean like finding papers or does it mean doing</p>	<p>1 front of you, it could like that, and be hard</p> <p>2 copies. It could be through, you know, an</p> <p>3 electronic mechanism, if there were something to</p> <p>4 share that way.</p> <p>5 Q All right. Did Medical Science</p> <p>6 Affiliates summarize any of those depositions that</p> <p>7 you have listed in your report?</p> <p>8 A I don't -- do I have -- I don't think --</p> <p>9 do I have deposition summaries?</p> <p>10 Q No.</p> <p>11 A Oh, then no.</p> <p>12 Q You have depositions.</p> <p>13 A Then the answer is no.</p> <p>14 Q Okay. Now, what you've provided me are</p> <p>15 reports and depositions of various experts either</p> <p>16 for Johnson & Johnson or for the plaintiff that</p> <p>17 you've indicated you've -- you've put them on your</p> <p>18 reliance list.</p> <p>19 And what I'm questioning is whether or</p> <p>20 not you've had any summaries done of those reports</p> <p>21 by Medical Science Affiliates.</p> <p>22 A No.</p> <p>23 Q Okay. Have they done any summaries of</p> <p>24 any type of information for you in the talcum</p> <p>25 powder products and ovarian cancer?</p>

42 (Pages 162 to 165)

Gregory B. Diette, M.D.

Page 166	Page 168
<p>1 MS. BROWN: And, Counsel, here I'm going</p> <p>2 to interject, and to the extent your question --</p> <p>3 MS. PARFITT: Objection. Form.</p> <p>4 MS. BROWN: -- seeks to -- I'm</p> <p>5 instructing on privilege, which I'm allowed to do</p> <p>6 under the federal rules and under the --</p> <p>7 MS. PARFITT: If it's a privilege</p> <p>8 issue --</p> <p>9 MS. BROWN: -- let me do that.</p> <p>10 MS. PARFITT: -- it's certainly fine.</p> <p>11 MS. BROWN: Thanks. So my instruction</p> <p>12 here will be that, Doctor, you are not under the</p> <p>13 work-product privilege to disclose any</p> <p>14 correspondence you've had with MSA, unless it is</p> <p>15 something on which you rely for your opinions</p> <p>16 here, and then of course, counsel is entitled to</p> <p>17 have that information.</p> <p>18 BY MS. PARFITT:</p> <p>19 Q With that understanding, how do you</p> <p>20 answer the question?</p> <p>21 A Can you say it again because I think I</p> <p>22 lost it?</p> <p>23 Q Sure. Let me just have it read back to</p> <p>24 you here.</p> <p>25 Has Medical Science Affiliates done any</p>	<p>1 Q Did you use for purposes of your expert</p> <p>2 report any of the summaries that were -- that were</p> <p>3 conducted by Medical Science Affiliates that you</p> <p>4 just spoke about?</p> <p>5 A See, this is where I -- I don't know if</p> <p>6 you're trying to confuse me or what, but --</p> <p>7 Q No, I'm not.</p> <p>8 A Okay. So I just want to be clear,</p> <p>9 because there aren't any summaries for this,</p> <p>10 right.</p> <p>11 Q Okay.</p> <p>12 A So -- and that's why I keep trying to --</p> <p>13 I just -- because there's a different answer for</p> <p>14 what -- what people have done in other matters and</p> <p>15 what they've done in this matter. There aren't</p> <p>16 any summaries that I'm aware of to -- to look at.</p> <p>17 Q All right. Did Medical Science</p> <p>18 Affiliates help you write your expert report?</p> <p>19 MS. BROWN: Objection to the form of the</p> <p>20 question.</p> <p>21 THE WITNESS: You know, "write" is a --</p> <p>22 is a word that can mean a lot of things. They</p> <p>23 helped me to -- to shape it, like to create the --</p> <p>24 the format for it and like edit out typos and</p> <p>25 things of that sort.</p>
Page 167	Page 169
<p>1 summaries of any type of information for you -- or</p> <p>2 provided any information for you on the talcum</p> <p>3 powder products and ovarian cancer cases?</p> <p>4 MS. BROWN: Same instruction. If you're</p> <p>5 relying on anything they've done, of course,</p> <p>6 please answer the question.</p> <p>7 THE WITNESS: So if we're talking about</p> <p>8 cases -- because that's why I clarified before,</p> <p>9 we're not talking about this matter. We're</p> <p>10 talking about ever in any -- in any case?</p> <p>11 BY MS. PARFITT:</p> <p>12 Q Ovarian cancer and talcum powder</p> <p>13 products.</p> <p>14 A Oh, yeah. No, I understand the words.</p> <p>15 I'm just trying to make sure whether we're talking</p> <p>16 about like this -- this matter that we're talking</p> <p>17 about only or -- or beyond that.</p> <p>18 Q Has -- has -- beyond that.</p> <p>19 A So I'm going to say probably they have.</p> <p>20 That if there are cases where there were like</p> <p>21 medical records, for example, although I don't</p> <p>22 think I've gotten any medical records, but they</p> <p>23 would have provided a summary. If there were</p> <p>24 deposition transcripts in those other cases, they</p> <p>25 might well have -- have done that.</p>	<p>1 BY MS. PARFITT:</p> <p>2 Q Okay. Well, that has -- it means a lot</p> <p>3 of things as well. So let me ask you --</p> <p>4 MS. BROWN: Counsel, just ask the</p> <p>5 question.</p> <p>6 MS. PARFITT: Counsel, I'm -- please.</p> <p>7 MS. BROWN: You can't editorialize like</p> <p>8 that. It's a question and an answer.</p> <p>9 BY MS. PARFITT:</p> <p>10 Q Dr. Diette, what I would like to ask you</p> <p>11 is, when you say they helped shape your report,</p> <p>12 what do you mean they helped shape your report?</p> <p>13 MS. BROWN: Objection.</p> <p>14 THE WITNESS: What I just said -- I mean</p> <p>15 what I said after -- after that before.</p> <p>16 BY MS. PARFITT:</p> <p>17 Q Is every word in your expert report that</p> <p>18 you have there in front of you a word that you put</p> <p>19 in it?</p> <p>20 MS. BROWN: Objection to the form.</p> <p>21 THE WITNESS: Well, I don't know. I</p> <p>22 mean, there's -- there's quotes from people,</p> <p>23 right, so that those aren't my words, for example.</p> <p>24 BY MS. PARFITT:</p> <p>25 Q Well, you know, I'm glad you brought</p>

43 (Pages 166 to 169)

Gregory B. Diette, M.D.

Page 170	Page 172
<p>1 that up. That's a good question.</p> <p>2 A Yeah.</p> <p>3 Q Are the opinions and the writings</p> <p>4 contained in that report words that you selected?</p> <p>5 A Oh, for sure. I mean like the opinions</p> <p>6 and my -- my summaries of things and -- is that</p> <p>7 what we're talking about?</p> <p>8 Q No. No.</p> <p>9 A We're not? All right.</p> <p>10 Q The report is about -- let's see how</p> <p>11 many pages -- it's about 51 pages long, and the</p> <p>12 question I have, with the exception of quotes from</p> <p>13 other people, Dr. Diette, is every word in this</p> <p>14 report a word you chose to put in the report?</p> <p>15 MS. BROWN: Objection to the form.</p> <p>16 THE WITNESS: For sure, yes. Although</p> <p>17 like some of the words, for example, I think might</p> <p>18 come from one of those affidavits that we were</p> <p>19 talking about, right. So it may be like, you</p> <p>20 know, words that I created in a different context</p> <p>21 and then pulled into this.</p> <p>22 BY MS. PARFITT:</p> <p>23 Q Okay. Well, then when you say "Medical</p> <p>24 Science Affiliates helped shape," I'm trying to</p> <p>25 get an understanding, what do you mean "shape"?</p>	<p>1 footnotes, like the information that comes from it</p> <p>2 was information that I pulled from the --</p> <p>3 Q Not my question. Who prepared the</p> <p>4 actual footnotes that appear at the bottom of your</p> <p>5 expert report of 58 -- or, excuse me, 51 pages?</p> <p>6 A So like actually put like -- like 110</p> <p>7 and then put like "Siemiatycki dep, 149"?</p> <p>8 Q Or how about put "226, Singh depo, don't</p> <p>9 consistently reduce," and there's a summary, I</p> <p>10 mean who provided that information, what staff?</p> <p>11 MS. BROWN: Objection to the form.</p> <p>12 Misstates his testimony about how the report was</p> <p>13 prepared.</p> <p>14 THE WITNESS: I'm sorry. We're looking</p> <p>15 at number 226.</p> <p>16 BY MS. PARFITT:</p> <p>17 Q By way of example, Dr. Diette.</p> <p>18 A No, no, I'm just -- I'm just trying to</p> <p>19 help because an example helps.</p> <p>20 So I don't know. I mean some -- some</p> <p>21 staff person put that particular -- literally that</p> <p>22 segment in, but like it came from me identifying</p> <p>23 that NSAIDS don't consistently reduce the risk of</p> <p>24 ovarian cancer and wanting to link it there to my</p> <p>25 statement.</p>
Page 171	Page 173
<p>1 A It would look like a disaster if I did</p> <p>2 this myself. So the fact that there are headings,</p> <p>3 that, you know, things don't spill over from one</p> <p>4 page to another. I don't remember if there's a</p> <p>5 table in here, but to not have the table split</p> <p>6 across, to have, you know, references look okay.</p> <p>7 That I'm not good at. So the fact that this, in</p> <p>8 my view, looks like a professional product, that's</p> <p>9 what they -- that's what they've done for me is to</p> <p>10 make it look like that.</p> <p>11 Q Okay. There are multiple footnotes in</p> <p>12 your report to testimony of various experts that</p> <p>13 were retained by the plaintiff.</p> <p>14 A Yeah.</p> <p>15 Q Who prepared those footnotes?</p> <p>16 MS. BROWN: Objection to the form.</p> <p>17 THE WITNESS: Staff somewhere, but --</p> <p>18 BY MS. PARFITT:</p> <p>19 Q I'm sorry.</p> <p>20 A Staff.</p> <p>21 Q Staff?</p> <p>22 A Yes.</p> <p>23 Q What staff?</p> <p>24 A I don't know which staff did it, but I</p> <p>25 mean like the -- if you say who prepared the</p>	<p>1 Q Who's the staff? Staff for MSA?</p> <p>2 A It could be MSA; it could be the law</p> <p>3 firm. I'm not sure which.</p> <p>4 Q Did you dictate to MSA or anyone else</p> <p>5 portions of your expert report, and someone else</p> <p>6 then did the recordation?</p> <p>7 A Somebody else did the --</p> <p>8 Q Did the -- did --</p> <p>9 A The --</p> <p>10 Q Did you dictate any portions of your</p> <p>11 report to anyone?</p> <p>12 A I don't -- I don't do that.</p> <p>13 Q You don't dictate. Okay.</p> <p>14 A No.</p> <p>15 Q Did you spend time on the phone with</p> <p>16 anyone at MSA and discuss what your -- your report</p> <p>17 should look like?</p> <p>18 MS. BROWN: And again, I'm going to</p> <p>19 instruct on work product, that you not reveal the</p> <p>20 substance of any discussions you had regarding</p> <p>21 drafts of this report. Whether or not there was a</p> <p>22 conversation is an appropriate question to answer.</p> <p>23 THE WITNESS: Sure.</p> <p>24 BY MS. PARFITT:</p> <p>25 Q You did?</p>

Gregory B. Diette, M.D.

Page 174	Page 176
<p>1 A Yes.</p> <p>2 Q So you had a conversation --</p> <p>3 A Yes.</p> <p>4 Q -- about the substance of your report,</p> <p>5 correct?</p> <p>6 MS. BROWN: Objection to the form.</p> <p>7 THE WITNESS: Oh, no, you just -- you</p> <p>8 said something else before that. What was the</p> <p>9 question before?</p> <p>10 MS. BROWN: Discuss what your report</p> <p>11 should look like.</p> <p>12 THE WITNESS: Yeah, that's different.</p> <p>13 BY MS. PARFITT:</p> <p>14 Q Okay.</p> <p>15 A You changed it to "substance." But I</p> <p>16 mean what it should look like is what I'm talking</p> <p>17 about. It was -- it should look good, right? And</p> <p>18 so there should be like, you know, bold headings</p> <p>19 and there should be spaces where they belong.</p> <p>20 Q What's the name of the contact person</p> <p>21 you interfaced with at MSA?</p> <p>22 A My main one is Maddie Petta --</p> <p>23 Pettenati.</p> <p>24 Q Okay. And how long have you worked with</p> <p>25 Maddie Pettenati?</p>	<p>1 at MSA to help you get your report in order?</p> <p>2 MS. BROWN: Objection to the form,</p> <p>3 misstates the testimony.</p> <p>4 THE WITNESS: I don't recall the amount</p> <p>5 of time. I mean whatever it took. Like some of</p> <p>6 it might be like a two-minute conversation to say</p> <p>7 like, you know, I want to move a section down or</p> <p>8 something. Or, you know, Can you proofread that</p> <p>9 particular paragraph and look for typos? And</p> <p>10 things of that sort.</p> <p>11 BY MS. PARFITT:</p> <p>12 Q Did any of the folks at MSA make any</p> <p>13 suggestions with regard to the scientific or</p> <p>14 medical content of your report?</p> <p>15 MS. BROWN: Objection. Instruct not to</p> <p>16 answer on work product. You can discuss -- you</p> <p>17 can answer the question of whether you had any</p> <p>18 conversations, the substance of which is</p> <p>19 privileged, and I'll instruct you not to answer.</p> <p>20 MS. PARFITT: MSA is a third-party</p> <p>21 contractor from what I'm understanding.</p> <p>22 MS. BROWN: No different than if he was</p> <p>23 working with a secretary to format this.</p> <p>24 Conversations about drafts of the report are</p> <p>25 privileged and will not be discussed.</p>
Page 175	Page 177
<p>1 A A couple of years.</p> <p>2 Q Okay. Do you work with anyone else over</p> <p>3 at MSA to help you with your reports?</p> <p>4 A Oh, sure.</p> <p>5 MS. BROWN: Objection to the form.</p> <p>6 THE WITNESS: Yeah.</p> <p>7 BY MS. PARFITT:</p> <p>8 Q Who?</p> <p>9 A There's a woman named April, Shannon.</p> <p>10 I'm sure there's others too.</p> <p>11 Q What are their backgrounds?</p> <p>12 MS. BROWN: Objection to the form.</p> <p>13 THE WITNESS: Everybody has a -- a</p> <p>14 science background of some sort, like biology</p> <p>15 degrees, things of that sort.</p> <p>16 BY MS. PARFITT:</p> <p>17 Q Okay. How much time did you spend with</p> <p>18 the folks at -- the team at MSA for purposes of</p> <p>19 getting your report put together?</p> <p>20 A I don't know. I mean, what do you mean</p> <p>21 by "with"?</p> <p>22 Q Well, we know you've had conversations.</p> <p>23 We know that you have received information with</p> <p>24 regard to shaping your report, and what I want to</p> <p>25 know is, how much time did you spend with the team</p>	<p>1 BY MS. PARFITT:</p> <p>2 Q Doctor, if you can answer the question.</p> <p>3 A Can you say it again? I'm sorry.</p> <p>4 Q Sure. No worries. I'm just getting it</p> <p>5 here.</p> <p>6 Did any of the folks at MSA make any</p> <p>7 suggestions with regard to the scientific or</p> <p>8 medical content of your report?</p> <p>9 MS. BROWN: I'm instructing you not to</p> <p>10 answer that question under the work-product</p> <p>11 privilege.</p> <p>12 BY MS. PARFITT:</p> <p>13 Q Do you keep time records of the time you</p> <p>14 spend with MSA?</p> <p>15 A No.</p> <p>16 Q Okay. Well, I believe you testified at</p> <p>17 the beginning of your deposition that your charge</p> <p>18 per hour is \$485, correct?</p> <p>19 A Well, I was trying -- I was trying to</p> <p>20 make you understand that differently, and you said</p> <p>21 we would talk about it, so maybe we can. My</p> <p>22 charge is \$400 an hour.</p> <p>23 Q All right. Where does the 485 come</p> <p>24 from?</p> <p>25 A It's what I said before, right. They</p>

45 (Pages 174 to 177)

Gregory B. Diette, M.D.

Page 178	Page 180
<p>1 add \$85 when they bill somebody for my time.</p> <p>2 Q Who "they"?</p> <p>3 A MSA.</p> <p>4 Q "They," MSA?</p> <p>5 A Yeah.</p> <p>6 Q All right. So that I get it straight,</p> <p>7 you charge 400 -- \$400 for your time, correct?</p> <p>8 A Correct.</p> <p>9 Q And then your understanding is MSA</p> <p>10 charges an additional \$85 to someone for their</p> <p>11 assistance for you, correct?</p> <p>12 MS. BROWN: Objection to the form, calls</p> <p>13 for speculation.</p> <p>14 THE WITNESS: So it's -- I don't know --</p> <p>15 I don't know how they break it down, because they</p> <p>16 bill for different things, like they bill for</p> <p>17 photocopying, they bill for some administrative</p> <p>18 tasks separately. Whatever it is, it's their</p> <p>19 business model, and they -- they add that amount</p> <p>20 to the hourly rate.</p> <p>21 BY MS. PARFITT:</p> <p>22 Q How much did Medical Science bill for</p> <p>23 their work, do you know?</p> <p>24 MS. BROWN: Objection. Calls for</p> <p>25 speculation.</p>	<p>1 and basically an amount. I don't have --</p> <p>2 A Like it --</p> <p>3 Q -- it's been blacked out.</p> <p>4 A It doesn't matter. I can still --</p> <p>5 MS. BROWN: It's been redacted for work</p> <p>6 product.</p> <p>7 THE WITNESS: I mean I can help you</p> <p>8 understand it if you want.</p> <p>9 BY MS. PARFITT:</p> <p>10 Q All I really want to understand and get</p> <p>11 a better understanding, Dr. Diette, is the types</p> <p>12 of services that MSA provided you in order to</p> <p>13 file this -- prepare this report.</p> <p>14 A Yeah, I -- I listed those.</p> <p>15 Q Okay. Do they help you with all of your</p> <p>16 expert reports?</p> <p>17 A In what?</p> <p>18 Q Does MSA provide any type of service in</p> <p>19 any and all expert reports that you prepare in the</p> <p>20 context of litigation?</p> <p>21 A No.</p> <p>22 Q Okay. Do you have another go-to service</p> <p>23 to help you with the preparation of your expert</p> <p>24 services?</p> <p>25 MS. BROWN: Objection to form.</p>
Page 179	Page 181
<p>1 THE WITNESS: You can tell if we look at</p> <p>2 the -- the invoices.</p> <p>3 BY MS. PARFITT:</p> <p>4 Q Okay. They would bill the same number</p> <p>5 of -- well, let me ask for a clarification. Not</p> <p>6 all your work was done in conjunction with the</p> <p>7 assistance of Medical Science Affiliates, correct?</p> <p>8 MS. BROWN: Objection to the form.</p> <p>9 THE WITNESS: I mostly sat by myself.</p> <p>10 Yeah.</p> <p>11 BY MS. PARFITT:</p> <p>12 Q Okay. So the invoices that I have for</p> <p>13 you would not necessarily reflect all of the work</p> <p>14 that Medical Science Affiliates afforded you,</p> <p>15 correct?</p> <p>16 A That's incorrect.</p> <p>17 MS. BROWN: Objection to the form.</p> <p>18 BY MS. PARFITT:</p> <p>19 Q Okay.</p> <p>20 A I mean that's what I was trying to offer</p> <p>21 you earlier is to try to understand the -- the</p> <p>22 bills. Because also when you add that comment</p> <p>23 about the amount of money in total, it wasn't all</p> <p>24 money that goes to me.</p> <p>25 Q Yeah. The bills that I have have a date</p>	<p>1 THE WITNESS: No. I do stuff on my own</p> <p>2 as well.</p> <p>3 BY MS. PARFITT:</p> <p>4 Q All right. So there are cases where</p> <p>5 you've done the work by yourself, and there are</p> <p>6 cases like this particular case where you engage</p> <p>7 the services of MSA, correct?</p> <p>8 A That is --</p> <p>9 MS. BROWN: Objection to the form.</p> <p>10 THE WITNESS: -- correct.</p> <p>11 BY MS. PARFITT:</p> <p>12 Q Okay. And did MSA edit any of your --</p> <p>13 any of your -- did MSA edit your expert report?</p> <p>14 A Yeah.</p> <p>15 Q Okay. What kind of edits did they make?</p> <p>16 A Well, all sorts. Like I asked them to</p> <p>17 look for typos, for example.</p> <p>18 Q Right.</p> <p>19 A I just happen to be open to page 30 and</p> <p>20 31, and where you see that the -- there's like</p> <p>21 bulleted sections, when I wrote that, it was just</p> <p>22 one long impenetrable paragraph, and so they were</p> <p>23 nice enough to sort of break it into some chunks</p> <p>24 so it would be easier to read.</p> <p>25 Q Okay. Bear with me if I asked this</p>

Gregory B. Diette, M.D.

Page 182	Page 184
<p>1 before, but did MSA ever suggest any new sentences 2 or study that you didn't previously insert in your 3 paper? 4 A I doubt a new study. It could be -- I 5 mean we worked -- we worked pretty hard to make 6 sure that I have the full list of studies, you 7 know, acknowledged, and so if there was something 8 I left off -- I mean I don't remember this 9 specifically for this, but that would be a normal 10 practice, right, like which is to say, you know, 11 Oh, I saw in your list of papers that there's a 12 Smith paper, should that be on here? Not them 13 going out and saying, Oh, I found a Smith paper, 14 would you like that on there? 15 Q But they might looked at yours and say, 16 You -- you missed a study. Fair? 17 A Oh, sure. 18 MS. BROWN: Objection to the form. 19 THE WITNESS: Yeah. 20 BY MS. PARFITT: 21 Q Okay. And they might look at your 22 report and say, You missed -- 23 I think what I'm getting at, Dr. Diette, 24 you described their efforts as generally 25 editorial. Is that fair?</p>	<p>1 Q And I'm not concerned about the format. 2 What I'm concerned about is the substance, 3 Dr. Diette, as you can appreciate. 4 MS. BROWN: Objection. 5 BY MS. PARFITT: 6 Q And so what I'm trying to -- to get some 7 clarity here is that, other than perhaps providing 8 you a study that you may have omitted from your 9 report, is there anything else that falls more in 10 the substantive area that they provided and 11 offered for you? 12 A I -- I think I've answered as best I 13 can. 14 Q Well, why don't we -- let's talk about 15 your contact with J&J. When did they first reach 16 out to you to talk with you about being an expert 17 to defend them in these lawsuits? 18 MS. BROWN: Objection to the form of the 19 question. 20 THE WITNESS: So they never asked me to 21 defend them. They -- they asked me to evaluate 22 the epidemiologic literature. 23 And just to be clear, because it seemed 24 like it was tripping us up before trying to talk 25 about this, when I talk about J&J, it's lawyers</p>
Page 183	Page 185
<p>1 MS. BROWN: Objection to the form. 2 THE WITNESS: I would say administrative 3 and editorial. 4 BY MS. PARFITT: 5 Q Okay. So we can agree that it's both 6 administrative and editorial? 7 MS. BROWN: Objection to the form. 8 THE WITNESS: Correct. 9 BY MS. PARFITT: 10 Q And as I appreciate, in addition to 11 perhaps providing you with a study or two that -- 12 or three, however number, that you might have 13 omitted, is there anything substantive like that 14 that they did for you for purposes of your expert 15 report? 16 A I insist that they don't. I tell them 17 that I don't want any intellectual input into 18 the -- to the stuff that we're working on. Like I 19 don't want their -- I don't even know if they have 20 opinions, but I don't want their opinions. I 21 literally want this to look like a professional 22 product, and I want to get it done in a way that I 23 can still spend my time -- my other professional 24 time on other things. So if I were to try to make 25 this look like this, it would take me forever.</p>	<p>1 that are working with J&J as opposed to somebody 2 from J&J per se. And so I'll leave it to you guys 3 to sort out what that -- what that means. 4 BY MS. PARFITT: 5 Q Fair enough. 6 A But -- but the first time would have 7 been a lawyer back in 2017 who asked if I would be 8 interested in reviewing the epidemiologic 9 literature. 10 Q Who was that lawyer? 11 A Jonathan Cooper. 12 Q Okay. Now, at the time that Jonathan -- 13 or Jonathan Cooper contacted you, did you -- were 14 you working with MSA? 15 A Obviously, because I said ten years, 16 and, you know, this was 2017. 17 Q Okay. Did you share with Jonathan 18 Cooper that you worked with this MSA company to 19 help you prepare your expert reports? 20 A He knew about it already, because I 21 think the reason he reached out to me is because 22 he was impressed with the work I had done in 23 other -- other cases. 24 Q Okay. Well, when he -- when you say he 25 was impressed with you, with the work that you've</p>

47 (Pages 182 to 185)

Gregory B. Diette, M.D.

Page 186	Page 188
<p>1 done, when he -- let me explore that a little bit.</p> <p>2 When he called you, did you tell him</p> <p>3 that you had previously worked with MSA to help</p> <p>4 you with your expert reports?</p> <p>5 A I didn't have to.</p> <p>6 Q He knew that.</p> <p>7 A Yes.</p> <p>8 Q Okay. How would Mr. Cooper have known</p> <p>9 that you worked with MSA before?</p> <p>10 MS. BROWN: Objection to the form, calls</p> <p>11 for speculation.</p> <p>12 MR. LOCKE: Objection.</p> <p>13 BY MS. PARFITT:</p> <p>14 Q If you know. Seems like you know.</p> <p>15 A Oh, I do. We had -- he and I had worked</p> <p>16 together on other cases.</p> <p>17 Q Okay. What other cases did you work</p> <p>18 with Mr. Cooper on?</p> <p>19 A They were asbestos-related cases with</p> <p>20 plastic or phenolics, like electrical equipment.</p> <p>21 Q Okay. And in those cases that you</p> <p>22 worked with Jonathan on -- or Mr. Cooper on, did</p> <p>23 you utilize the services of MSA as well to help</p> <p>24 you prepare your expert report in those cases?</p> <p>25 A I did.</p>	<p>1 Q Okay. Have they ever listed you on some</p> <p>2 type of website as a consultant for legal</p> <p>3 purposes?</p> <p>4 A Well, I see --</p> <p>5 MS. BROWN: Objection to the form,</p> <p>6 calls for speculation.</p> <p>7 THE WITNESS: -- Mr. Finch is here and</p> <p>8 he --</p> <p>9 THE REPORTER: Excuse me.</p> <p>10 THE WITNESS: Oh, sorry.</p> <p>11 MS. BROWN: Objection to the form, call</p> <p>12 for speculation. Thank you.</p> <p>13 THE WITNESS: Mr. Finch flashed</p> <p>14 something up at a trial to suggest that they had,</p> <p>15 but that wasn't an advertisement for me. It was a</p> <p>16 list of somebody who had credentials that were</p> <p>17 similar to mine.</p> <p>18 BY MS. PARFITT:</p> <p>19 Q Okay. Well, my question is, have -- are</p> <p>20 you aware of whether or not Medical Science</p> <p>21 Affiliates has ever advertised your name out in</p> <p>22 the -- the community as someone --</p> <p>23 MS. BROWN: Same objection --</p> <p>24 BY MS. PARFITT:</p> <p>25 Q -- who was a specialist in pulmonology</p>
Page 187	Page 189
<p>1 Q Okay. Has MSA reached out to you and</p> <p>2 engaged or asked if you would engage in assisting</p> <p>3 them on any other projects currently?</p> <p>4 A What do you mean by "currently"?</p> <p>5 Q Well, are you working with MSA on any</p> <p>6 other projects other than the talcum powder</p> <p>7 products and ovarian cancer?</p> <p>8 A Yes.</p> <p>9 Q What projects?</p> <p>10 MS. BROWN: And again, Doctor, to the</p> <p>11 extent that a confidentiality agreement doesn't</p> <p>12 prevent you from disclosing other work that you're</p> <p>13 doing, you can answer the question.</p> <p>14 THE WITNESS: Some cases that relate to</p> <p>15 asbestos and other chemical-related cases.</p> <p>16 BY MS. PARFITT:</p> <p>17 Q Okay. Was there a time when you,</p> <p>18 instead of receiving services from MSA, you</p> <p>19 provided services to MSA as an affiliate expert?</p> <p>20 MS. BROWN: Objection to the form of the</p> <p>21 question.</p> <p>22 THE WITNESS: I know they have that word</p> <p>23 "affiliate" in their name. I don't know what that</p> <p>24 means. But I don't provide services to them.</p> <p>25 BY MS. PARFITT:</p>	<p>1 medicine?</p> <p>2 MS. BROWN: Same objection.</p> <p>3 THE WITNESS: I'm not aware that they</p> <p>4 advertise.</p> <p>5 BY MS. PARFITT:</p> <p>6 Q Okay. So are there times that Medical</p> <p>7 Science Affiliates reaches out to you and says,</p> <p>8 Dr. Diette, we want you to do a medical -- a</p> <p>9 scientific review for us on a topic?</p> <p>10 A Never.</p> <p>11 Q Okay. They've never done that. You've</p> <p>12 never provided that service for them.</p> <p>13 A They -- they don't ask me to do work for</p> <p>14 them.</p> <p>15 Q Okay. Do their clients ask you to do</p> <p>16 work for them?</p> <p>17 A Of course, that's where we started,</p> <p>18 right, from ten years ago.</p> <p>19 Q Right. And that's what I'm trying to</p> <p>20 figure out.</p> <p>21 MS. BROWN: Let him finish. I don't</p> <p>22 think he was done.</p> <p>23 THE WITNESS: No, that was -- that was</p> <p>24 the description of what I was saying, like how</p> <p>25 the -- the first time that I met them was that</p>

48 (Pages 186 to 189)

Gregory B. Diette, M.D.

Page 190	Page 192
<p>1 they -- there was some, you know, group that 2 wanted an epidemiologic review, and they were 3 trying to figure out if there were local 4 epidemiologists that could take on a task like 5 that, and so that's the way it worked. 6 BY MS. PARFITT: 7 Q Okay. So I now get -- 8 MS. BROWN: He is not done. 9 BY MS. PARFITT: 10 Q Are you done, Doctor? I thought you 11 were. 12 A I'll be done. 13 Q Okay. So if I appreciate this 14 structure, so we can move on, a client, some 15 company can reach out to Medical Science 16 Affiliates and say, We need some work done and 17 research done on a particular area. Will you do 18 that for me? 19 Medical Science Affiliates will say, 20 Yes, we can. And then Medical Science Affiliates 21 reaches out to people like you? 22 MS. BROWN: Objection to the form. 23 THE WITNESS: So I don't know -- I don't 24 know when they say, Yes, we can. Like I don't 25 know, for example -- like their -- I don't know</p>	<p>1 Q So you never work for MSA; you always 2 work for a corporate client? 3 MR. LOCKE: Objection. 4 MS. BROWN: Objection to the form of the 5 question. 6 THE WITNESS: So I've never worked for 7 MSA. 8 BY MS. PARFITT: 9 Q Who pays your bills? Law firms? 10 MS. BROWN: Objection to the form. 11 THE WITNESS: So -- 12 MS. BROWN: What bills? What are you 13 talking about? 14 BY MS. PARFITT: 15 Q Who pays your bills for doing services 16 at the request of MSA? 17 MS. BROWN: Objection to the form. 18 BY MS. PARFITT: 19 Q Anybody? 20 MS. BROWN: Objection. Can we -- let's 21 have one question and let him answer. 22 Go ahead. 23 BY MS. PARFITT: 24 Q And I'll tell you the reason I'm asking, 25 Dr. Diette.</p>
Page 191	Page 193
<p>1 what their size is, but they may say, Yes, we can, 2 and just do it themselves. Right. They have 3 other people that I don't work with that work 4 there. 5 I'm just saying, like you're asking the 6 question, so it's like -- so if somebody calls 7 them and says, Can you do this work? They may 8 well say, Yes, we can do it. They may or may not 9 need a content expert or methodologic expert to do 10 it. So it -- I assume it depends, but I'm -- I'm 11 not familiar with their entire business operation. 12 BY MS. PARFITT: 13 Q Okay. All I'm trying to find out is -- 14 is who comes to who, and from what I understand 15 your testimony is, a client will reach out to MSA 16 and say, We have a project. MSA will determine 17 whether or not someone -- someone's expertise is 18 needed in order to complete that job, and then MSA 19 reaches out to you. Is that fair? 20 MR. LOCKE: Objection. 21 MS. BROWN: Objection. Speculation. 22 THE WITNESS: I like the answer I just 23 gave. I mean I think that really was my answer to 24 that exact question. 25 BY MS. PARFITT:</p>	<p>1 MS. BROWN: No, no, no, no. You ask the 2 question, he answers. We don't need to know why 3 you're asking the question. 4 MS. PARFITT: Excuse me. 5 MS. BROWN: It's improper. You're not 6 going to give a speech, Counsel. 7 BY MS. PARFITT: 8 Q Dr. Diette, we -- has there ever been a 9 chance or an opportunity where you have reached 10 out to MSA on your own, and say, A client that 11 doesn't work or do business with you, MSA, has 12 asked me to do a report. Can you help me? 13 A Yes. 14 Q Okay. So that's one scenario, correct? 15 A Correct. 16 Q It's some other client has -- some other 17 individual or entity has reached out to you and 18 said, Dr. Diette, I would like to engage your 19 expertise in the legal context. Fair? 20 MS. BROWN: Objection to the form. 21 THE WITNESS: Or the epidemiologic 22 context, but in some context. 23 BY MS. PARFITT: 24 Q Okay. And then you have in turn reached 25 out to MSA and said, I need some help.</p>

Gregory B. Diette, M.D.

Page 194	Page 196
<p>1 MS. BROWN: Objection to the form.</p> <p>2 THE WITNESS: Something like that, yeah.</p> <p>3 BY MS. PARFITT:</p> <p>4 Q Okay. That's one scenario.</p> <p>5 Another scenario is when a corporate</p> <p>6 client, for instance, engages the services of MSA</p> <p>7 to do a project and a particular expertise is</p> <p>8 needed, and MSA then reaches out to folks like</p> <p>9 yourself or folks in other medical specialties.</p> <p>10 Fair?</p> <p>11 MS. BROWN: Objection. Speculation.</p> <p>12 THE WITNESS: So I'm not a lawyer,</p> <p>13 right. So I'm trying to listen carefully to the</p> <p>14 words that you're using, and when you say they</p> <p>15 reach out and they retain MSA, I -- I actually</p> <p>16 don't know if that's actually what happens, right.</p> <p>17 So I gave you an example that --</p> <p>18 BY MS. PARFITT:</p> <p>19 Q Okay.</p> <p>20 A -- they might retain MSA for their own</p> <p>21 purposes, and nobody else gets involved. If like,</p> <p>22 for example, in this case when Jonathan Cooper</p> <p>23 reached out, he wanted to work with me, and MSA</p> <p>24 provided the support services for me to get that</p> <p>25 work done. So I -- I have no idea whether he</p>	<p>1 conflicts checks?</p> <p>2 MS. BROWN: Objection. Speculation.</p> <p>3 Engaged by who?</p> <p>4 BY MS. PARFITT:</p> <p>5 Q When you're engaged by a client, who</p> <p>6 does the conflict --</p> <p>7 MS. BROWN: Same --</p> <p>8 BY MS. PARFITT:</p> <p>9 Q -- conflicts checks for you?</p> <p>10 MS. BROWN: Same objection.</p> <p>11 THE WITNESS: I don't know that anybody</p> <p>12 does conflicts checks. I mean if there is</p> <p>13 somebody, I'm not aware of who that is. If it</p> <p>14 comes up, people will ask me sometimes if I have a</p> <p>15 conflict of interest. Sometimes I'll see a</p> <p>16 complaint, you know, and be asked to look at, you</p> <p>17 know, the names on the complaint.</p> <p>18 It all depends, but I -- I don't even</p> <p>19 know if I know what a conflict checks is, I mean</p> <p>20 if that's a technical term. It's only been --</p> <p>21 it's only been done the way I'm describing, which</p> <p>22 somebody will say to me like, you know, Do you</p> <p>23 have any conflict of interest?</p> <p>24 BY MS. PARFITT:</p> <p>25 Q Okay. You prepared two affidavits that</p>
Page 195	Page 197
<p>1 retained MSA per se. I mean that's -- that's</p> <p>2 something for lawyers to kind of sort through.</p> <p>3 Q Well, did Jonathan Cooper go to you</p> <p>4 directly or did Jonathan Cooper go to MSA?</p> <p>5 MS. BROWN: Objection to the form.</p> <p>6 You can answer if you know.</p> <p>7 THE WITNESS: It was kind of both. I</p> <p>8 mean I think we -- we were talking about something</p> <p>9 else one day, and he asked if I would be</p> <p>10 interested in this.</p> <p>11 BY MS. PARFITT:</p> <p>12 Q Okay. And did Jonathan Cooper then</p> <p>13 reach out to MSA as well?</p> <p>14 MS. BROWN: Objection. Speculation.</p> <p>15 BY MS. PARFITT:</p> <p>16 Q You said both. That's why I'm asking.</p> <p>17 A Yeah, yeah, I mean --</p> <p>18 MS. BROWN: Same objection.</p> <p>19 THE WITNESS: I don't know how that part</p> <p>20 worked, I mean, but -- but it was pretty clear</p> <p>21 that it was such a big volume of work, that if I</p> <p>22 was going to do it with him that I was going to</p> <p>23 use MSA's services.</p> <p>24 BY MS. PARFITT:</p> <p>25 Q When you're engaged, who does the</p>	<p>1 I'm aware of, one in the Ingham case and one in</p> <p>2 the Forrest. Do you recall doing that back in</p> <p>3 2018?</p> <p>4 A I do.</p> <p>5 Q Okay. Are you aware of any other</p> <p>6 affidavits you prepared in 2018 other than the</p> <p>7 Ingham and the Forrest?</p> <p>8 A I don't think so. But I mean if you</p> <p>9 have one, I would be glad to help confirm it, but</p> <p>10 I can't recall one off the top of my head.</p> <p>11 Q Fair enough. How much did you charge</p> <p>12 for preparation of the Ingham affidavit?</p> <p>13 MS. BROWN: Objection to the form.</p> <p>14 THE WITNESS: I don't remember.</p> <p>15 BY MS. PARFITT:</p> <p>16 Q More than 50,000?</p> <p>17 MS. BROWN: Same objection.</p> <p>18 THE WITNESS: So I guess it depends upon</p> <p>19 when we're talking about like me, you know,</p> <p>20 because earlier you were lumping together, you</p> <p>21 know, services that MSA charges for and gets paid</p> <p>22 for. So I don't remember what -- what part I got.</p> <p>23 It wouldn't -- it wouldn't have taken \$50,000</p> <p>24 worth of my time to prepare, you know, the</p> <p>25 affidavit, I don't think. And in part, because,</p>

50 (Pages 194 to 197)

Gregory B. Diette, M.D.

Page 198	Page 200
<p>1 you know, the input for that was stuff I was 2 already, you know, reading and interpreting 3 otherwise. 4 BY MS. PARFITT: 5 Q All right. How much did you charge for 6 the Forrest report? 7 MS. BROWN: Objection to the form. 8 THE WITNESS: The same -- same answer. 9 I don't know. And in fact, the Forrest report, if 10 it came second, probably not very much because I 11 think it's mostly derivative from the first. I 12 mean I try -- I'm not trying to just, you know, 13 create work to create it. Like if there's 14 something I -- that I like the way it reads, I try 15 to use it again. 16 BY MS. PARFITT: 17 Q Okay. Are you aware, having actually 18 prepared both of those affidavits, they are 19 virtually the same affidavit? Would that surprise 20 you? 21 MS. BROWN: Objection to the form. 22 THE WITNESS: I hope they are. I mean 23 that -- that was the intent. 24 BY MS. PARFITT: 25 Q Okay. Other than the ovarian cancer/</p>	<p>1 products and ovarian cancer. 2 And the question I have is, in any 3 context, when the topic of interest is talcum 4 powder products and ovarian cancer, have you ever 5 been asked by MSA to do any work that's 6 non-pulmonary, other than the ovarian cancer 7 cases? 8 A Related -- 9 MR. LOCKE: Objection. 10 THE WITNESS: Related to talcum powder? 11 BY MS. PARFITT: 12 Q Related to anything. 13 A Well, wait a minute. No, because -- so, 14 first of all, you said has MSA asked me to do it. 15 Like they don't ask me to do stuff. Like they -- 16 it's -- the relationship we described before is 17 what it is. So if it's more general about are 18 there other cases -- 19 Q Yeah. 20 A -- and when you say non-pulmonary, you 21 know, there are cases I've been involved in that 22 have nothing do with talcum powder that are 23 non-pulmonary. 24 So I'm just trying to figure out, 25 there's a lot of different angles to what -- to</p>
Page 199	Page 201
<p>1 talcum powder cases, have you been engaged by 2 anyone else for opinions on a non-pulmonary issue? 3 MS. BROWN: Objection to the form. 4 THE WITNESS: Related to? 5 BY MS. PARFITT: 6 Q Your work with MSA. 7 A No, but you said -- it sounded like 8 there's something missing from the question. 9 Q Sure. Let me -- let me ask it again. 10 Okay. 11 Other than this case involving ovarian 12 cancer and talcum powder products, have you been 13 asked and -- or requested by anyone for your 14 opinions on a topic that was something other than 15 non-pulmonary? 16 MS. BROWN: Objection. Do you mean -- 17 MS. PARFITT: That was non-pulmonary. 18 MS. BROWN: -- to exclude Ingham and the 19 other? When you say "this case," do you mean just 20 the MDL? 21 MS. PARFITT: Yeah. 22 BY MS. PARFITT: 23 Q And I think that's where we're getting 24 hung up. When I say "this case," I'm going to be 25 talking about "this case" being talcum powder</p>	<p>1 what you're asking. 2 Q Sure. 3 A Are you talking about talcum powder 4 cases that are related to something other than 5 ovarian cancer, and something other than a 6 pulmonary -- 7 Q I'll simplify it. Have you ever 8 prepared a report in a -- let me do it this way. 9 Talcum powder products and ovarian 10 cancer have nothing to do with pulmonary medicine, 11 correct? 12 MS. BROWN: Objection to the form. Are 13 we abandoning inhalation as a theory of -- 14 MS. PARFITT: No, we're not, no. 15 MS. BROWN: Okay. 16 THE WITNESS: Then no. I mean, no, 17 meaning that if that's a theory, then that 18 certainly has something to do with pulmonary 19 medicine. 20 BY MS. PARFITT: 21 Q Okay. And I think what I'm really 22 driving at is, it looks as though your focus for 23 the last couple of years has been talcum powder 24 products and ovarian cancer or asbestos and 25 mesothelioma. Is that fair?</p>

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 202</p> <p>1 MR. LOCKE: Objection.</p> <p>2 THE WITNESS: My focus --</p> <p>3 BY MS. PARFITT:</p> <p>4 Q Focus and research --</p> <p>5 MS. BROWN: Objection.</p> <p>6 BY MS. PARFITT:</p> <p>7 Q -- for preparation of expert legal</p> <p>8 reports.</p> <p>9 MS. BROWN: Objection to the form.</p> <p>10 THE WITNESS: I -- I'm either not</p> <p>11 hearing you well or I think things are getting</p> <p>12 jumbled.</p> <p>13 BY MS. PARFITT:</p> <p>14 Q Okay.</p> <p>15 A And I --</p> <p>16 Q Probably the -- the latter.</p> <p>17 A No, and I apologize.</p> <p>18 Q It's probably me.</p> <p>19 A I'm not trying to give you a hard time.</p> <p>20 I just mean that -- what I -- what I heard earlier</p> <p>21 is am I working on something with talcum powder</p> <p>22 other than ovarian cancer or other than ovarian</p> <p>23 cancer and something that isn't part of the lung?</p> <p>24 Is that it?</p> <p>25 Q Are you preparing expert reports on a</p>	<p style="text-align: right;">Page 204</p> <p>1 anything --</p> <p>2 Q Do you want to take --</p> <p>3 A No, I'm just wondering. Not</p> <p>4 necessarily, but if it's --</p> <p>5 MS. MILLER: This would be a good time</p> <p>6 for lunch.</p> <p>7 THE WITNESS: Yeah, that's what I'm</p> <p>8 wondering, just if it's going to be --</p> <p>9 MS. BROWN: Yeah, it's up to you. If</p> <p>10 you want to break, counsel will give you a break.</p> <p>11 MS. PARFITT: Whatever you want to do.</p> <p>12 Do you want to take a break now?</p> <p>13 THE WITNESS: It would be nice to -- to</p> <p>14 get a snack, and --</p> <p>15 MS. PARFITT: You want to take a half</p> <p>16 hour and grab --</p> <p>17 THE WITNESS: Would that be okay?</p> <p>18 MS. PARFITT: That's totally fine, yep.</p> <p>19 THE VIDEOGRAPHER: The time is 12:08</p> <p>20 p.m., and we are going off the record.</p> <p>21 (Lunch recess.)</p> <p>22 THE VIDEOGRAPHER: The time is 12:43</p> <p>23 p.m., and we're back on the record.</p> <p>24 BY MS. PARFITT:</p> <p>25 Q Good afternoon, Dr. Diette.</p>
<p style="text-align: right;">Page 203</p> <p>1 topic area other than talcum powder products and</p> <p>2 ovarian cancer currently?</p> <p>3 MS. BROWN: Objection. He's not</p> <p>4 answering questions about reports that have not</p> <p>5 been served in cases --</p> <p>6 MS. PARFITT: Understood.</p> <p>7 MS. BROWN: -- where he's not a</p> <p>8 disclosed expert.</p> <p>9 THE WITNESS: You mean in my</p> <p>10 professional life in general?</p> <p>11 BY MS. PARFITT:</p> <p>12 Q Correct.</p> <p>13 A Yes.</p> <p>14 Q Okay. What other areas?</p> <p>15 A Well, that's what we talked about</p> <p>16 before, right. So there was asbestos, there's</p> <p>17 some chemicals, probably like mold and dampness.</p> <p>18 There's malpractice cases. I mean a whole variety</p> <p>19 of different things.</p> <p>20 Q Okay. All right. I want to come to --</p> <p>21 where I want to go is your -- your actual report.</p> <p>22 I want you to take me through -- I'll ask you some</p> <p>23 questions about the process that you went through</p> <p>24 in actually putting this report together.</p> <p>25 A And I don't want to overbreak or</p>	<p style="text-align: right;">Page 205</p> <p>1 A Good afternoon.</p> <p>2 Q All right, Dr. Diette, I'd like to focus</p> <p>3 for a little bit about your -- actually your</p> <p>4 expert report and hopefully get to your opinions</p> <p>5 here soon.</p> <p>6 It's fair to say that this report is --</p> <p>7 this expert report is not a report that you</p> <p>8 prepared in the ordinary course of your activities</p> <p>9 as a pulmonary medicine at Johns Hopkins?</p> <p>10 MS. BROWN: Objection to the form.</p> <p>11 THE WITNESS: That's correct.</p> <p>12 BY MS. PARFITT:</p> <p>13 Q Okay. And are all the opinions which</p> <p>14 you will be sharing with us today, and eventually</p> <p>15 the court and a jury, set forth in your -- your</p> <p>16 expert report?</p> <p>17 MS. BROWN: Form.</p> <p>18 THE WITNESS: I hope so. I mean,</p> <p>19 it's -- there may be like -- like smaller opinions</p> <p>20 that are underpinnings that I didn't capture, but</p> <p>21 I mean the fundamental opinions should be there.</p> <p>22 And assuming nothing different comes out when</p> <p>23 you're asking me about it today, I guess the only</p> <p>24 other thing I'd say is that I don't think that</p> <p>25 I've seen all of the -- the testimony yet in this</p>

Gregory B. Diette, M.D.

Page 206	Page 208
<p>1 case. So I don't know whether that's going to,</p> <p>2 you know, spur some other thought, you know, from</p> <p>3 the other -- other experts who are testifying, but</p> <p>4 aside from that, then this should otherwise be</p> <p>5 complete.</p> <p>6 BY MS. PARFITT:</p> <p>7 Q And obviously if you see something,</p> <p>8 testimony that causes you to change your opinions,</p> <p>9 you will let me know, correct?</p> <p>10 MS. BROWN: Form.</p> <p>11 THE WITNESS: I will.</p> <p>12 BY MS. PARFITT:</p> <p>13 Q All right. Dr. Diette, on the front of</p> <p>14 your report it says "Expert Report of Gregory</p> <p>15 Diette, MD, MHS, For General Causation Daubert</p> <p>16 Hearing." Did you write that?</p> <p>17 A Not this page, no.</p> <p>18 Q All right. Who wrote that?</p> <p>19 MS. BROWN: Objection to the form.</p> <p>20 THE WITNESS: I -- I don't know</p> <p>21 literally. I think this came from the law firm as</p> <p>22 a cover page for me to -- to sign.</p> <p>23 BY MS. PARFITT:</p> <p>24 Q You've testified both in general</p> <p>25 causation case -- as a general causation witness</p>	<p>1 to say that that is your signature on the -- on</p> <p>2 the front page, Gregory Diette?</p> <p>3 A Yes, it is.</p> <p>4 Q And you completed that on February 25th,</p> <p>5 2019, correct?</p> <p>6 A Exactly right.</p> <p>7 Q Okay. And it would also -- is it also</p> <p>8 fair to say that the opinions contained in this</p> <p>9 report are not the opinions of Johns Hopkins</p> <p>10 University?</p> <p>11 A Not as far as I know. I mean they're</p> <p>12 literally just mine.</p> <p>13 Q Have you shared these opinions with any</p> <p>14 of the other members of the Johns Hopkins</p> <p>15 community?</p> <p>16 A No.</p> <p>17 Q All right. Did you run the opinions</p> <p>18 that you have by any of the staff or your</p> <p>19 superiors at Johns Hopkins?</p> <p>20 MS. BROWN: Objection to the form.</p> <p>21 THE WITNESS: No.</p> <p>22 BY MS. PARFITT:</p> <p>23 Q Okay. Aside from this expert report and</p> <p>24 the opinions retained herein, have you shared your</p> <p>25 opinions with anyone else outside of the Johns</p>
Page 207	Page 209
<p>1 and as well as a specific causation witness,</p> <p>2 correct?</p> <p>3 A Generally speaking, like in legal cases?</p> <p>4 Q Correct.</p> <p>5 A Yes, I have.</p> <p>6 Q All right. So you understand the</p> <p>7 difference.</p> <p>8 A I hope so, yeah.</p> <p>9 Q Okay. Have you actually testified in an</p> <p>10 asbestos/meso- -- mesothelioma case on giving</p> <p>11 specific causation opinions?</p> <p>12 A Yes.</p> <p>13 Q Okay. Have you also provided general</p> <p>14 causation opinions in a meso/asbestos case?</p> <p>15 A Yes.</p> <p>16 Q Okay. Now, it says Daubert. Do you</p> <p>17 understand what a Daubert hearing is?</p> <p>18 MS. BROWN: Objection to the form.</p> <p>19 THE WITNESS: Probably not the way that</p> <p>20 you do. I have a general -- general sense of</p> <p>21 this, but -- you know, I -- I wouldn't be able to</p> <p>22 answer, you know, a lot of test questions about</p> <p>23 it.</p> <p>24 BY MS. PARFITT:</p> <p>25 Q Okay. All right. And would it be fair</p>	<p>1 Hopkins community, regulatory or scientific</p> <p>2 bodies?</p> <p>3 MS. BROWN: Objection to the form.</p> <p>4 THE WITNESS: No. You mean other than</p> <p>5 the lawyers and --</p> <p>6 BY MS. PARFITT:</p> <p>7 Q Correct, other than your lawyers.</p> <p>8 A Oh, yeah, yeah, yeah.</p> <p>9 MS. BROWN: Objection to the form.</p> <p>10 We're not his lawyers.</p> <p>11 THE WITNESS: Right, but I mean but</p> <p>12 lawyers that are involved in this case, I have</p> <p>13 expressed it to, but not those other kinds of</p> <p>14 entities that you described.</p> <p>15 BY MS. PARFITT:</p> <p>16 Q Okay. And to be clear, you have not</p> <p>17 shared with the Johns Hopkins community your</p> <p>18 opinions on talcum powder products and ovarian</p> <p>19 cancer.</p> <p>20 MS. BROWN: Objection to the form.</p> <p>21 THE WITNESS: That is correct.</p> <p>22 BY MS. PARFITT:</p> <p>23 Q Okay. Let's go to I believe page 2 of</p> <p>24 your report, if you will.</p> <p>25 And take a moment. Do you have that in</p>

Gregory B. Diette, M.D.

Page 210	Page 212
<p>1 front of you?</p> <p>2 A I do. Thank you.</p> <p>3 Q Okay. Is it fair to say that your</p> <p>4 report contains the bases for your opinions as</p> <p>5 well?</p> <p>6 A Yes.</p> <p>7 Q All right. And is it fair the -- do you</p> <p>8 know whether or not this report has answered all</p> <p>9 the questions that J&J asked you to answer for</p> <p>10 them?</p> <p>11 MS. BROWN: Objection. Lacks</p> <p>12 foundation.</p> <p>13 THE WITNESS: Well, I think there's only</p> <p>14 one question, right?</p> <p>15 BY MS. PARFITT:</p> <p>16 Q And what was that question?</p> <p>17 MS. BROWN: Wait. Let him finish.</p> <p>18 BY MS. PARFITT:</p> <p>19 Q What was that question?</p> <p>20 A I'm sorry. So the question was -- was</p> <p>21 really about whether or not the -- what does the</p> <p>22 epidemiologic evidence say about the relationship</p> <p>23 between talcum powder and ovarian cancer.</p> <p>24 Q All right. So let's turn to your</p> <p>25 report, page 2, and I believe --</p>	<p>1 Q Okay. And if you would turn -- be so</p> <p>2 kind to turn to the last page of the report,</p> <p>3 page 51.</p> <p>4 A Okay.</p> <p>5 Q And again, if you would read the first</p> <p>6 paragraph.</p> <p>7 A At the --</p> <p>8 Q And we'll go ahead and put that up on</p> <p>9 the ELMO.</p> <p>10 A Under "Conclusion" or the --</p> <p>11 Q Under the Conclusion, if you will.</p> <p>12 A Yep. The whole thing?</p> <p>13 Q Just that -- just that first</p> <p>14 paragraph -- or first sentence.</p> <p>15 A First sentence. Oh, okay. Yep.</p> <p>16 "It is my opinion, based on my</p> <p>17 qualifications and my extensive review of the</p> <p>18 available epidemiology studies and scientific</p> <p>19 literature, that there is not sufficient evidence</p> <p>20 to conclude that there is a causal relationship</p> <p>21 between perineal talcum powder exposure and</p> <p>22 ovarian cancer."</p> <p>23 Q Okay. And I know you have much to say</p> <p>24 about that, but that is basically the -- the</p> <p>25 general opinion that you're going to be sharing,</p>
Page 211	Page 213
<p>1 MS. PARFITT: And we'll put it up on the</p> <p>2 ELMO here.</p> <p>3 (Counsel conferring.)</p> <p>4 MS. PARFITT: I guess we won't put it up</p> <p>5 on the ELMO here.</p> <p>6 BY MS. PARFITT:</p> <p>7 Q Looking at the Summary of Opinions,</p> <p>8 would you please read, if you will, that first</p> <p>9 sentence.</p> <p>10 A Down at the bottom?</p> <p>11 Q Please.</p> <p>12 A "The body of"?</p> <p>13 Q Under "Summary of Opinions."</p> <p>14 A Yep, sure.</p> <p>15 "The body of relevant epidemiological</p> <p>16 evidence does not support a causal connection</p> <p>17 between perineal use of talcum powder products,"</p> <p>18 parentheses, "whatever constituents those products</p> <p>19 may contain in addition to talc," end parentheses,</p> <p>20 "and ovarian cancer."</p> <p>21 Q All right. And then in the next page is</p> <p>22 you talk about the bases for that, correct?</p> <p>23 A I think that's the right way to say the</p> <p>24 bases. I mean it's sort of an elaboration of that</p> <p>25 general -- general opinion.</p>	<p>1 correct?</p> <p>2 A I agree with you, yes.</p> <p>3 Q Okay. Let me show you what we'll have</p> <p>4 marked as 12, Exhibit 12.</p> <p>5 (Counsel conferring.)</p> <p>6 MS. PARFITT: Let me show you, Counsel,</p> <p>7 what we -- what we'll have marked as Exhibit 12.</p> <p>8 There you go.</p> <p>9 (Diette Exhibit No. 12 was marked</p> <p>10 for identification.)</p> <p>11 BY MS. PARFITT:</p> <p>12 Q Doctor, have you seen this before?</p> <p>13 A Let me take a look and see. (Peruses</p> <p>14 document.)</p> <p>15 So generally speaking, yes. The -- the</p> <p>16 only reason I can't say for sure I've literally</p> <p>17 seen this exact version is because that -- not</p> <p>18 that I would know when it was updated otherwise,</p> <p>19 but I don't know who's in charge of all these</p> <p>20 different -- excuse me -- websites that you found</p> <p>21 at Johns Hopkins, and so I don't know, you know,</p> <p>22 whether what I looked at is literally identical to</p> <p>23 what we're looking at here.</p> <p>24 Q All right.</p> <p>25 A But it's approximately something that</p>

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 214</p> <p>1 I've seen.</p> <p>2 Q Okay. Fair.</p> <p>3 Now, this is from the Sidney Kimmel</p> <p>4 Comprehensive Cancer Center, correct?</p> <p>5 A That's right.</p> <p>6 Q And it's entitled "Risk Factors -- Risk</p> <p>7 Factors" -- excuse me -- and Symptoms." Do you</p> <p>8 see that?</p> <p>9 A I do.</p> <p>10 Q All right. And if you and this is for</p> <p>11 ovarian cancer, you see that?</p> <p>12 On the second line, "ovarian cancer," it</p> <p>13 talks --</p> <p>14 A Yes.</p> <p>15 Q Okay. Now, what I'd like you to do is</p> <p>16 turn to the second page, and there is a risk</p> <p>17 factor listed, amongst others. Do you see that?</p> <p>18 A I do.</p> <p>19 Q And it says "Talcum Powder and</p> <p>20 Asbestos." Do you see that?</p> <p>21 A Yes.</p> <p>22 Q All right. Would you read that, please.</p> <p>23 A "Habitual use of talcum powder on the</p> <p>24 genital area may increase the risk for ovarian</p> <p>25 cancer, but the evidence is not strong. A study"</p>	<p style="text-align: right;">Page 216</p> <p>1 up here, and I'm going to doc- -- and I'm going to</p> <p>2 go ahead and make a notation as you talk, and</p> <p>3 we're going to put your initials by that which you</p> <p>4 agree or don't agree, or that which resonates with</p> <p>5 you or that which does not.</p> <p>6 So give me a moment. Hang with me,</p> <p>7 okay?</p> <p>8 A Yeah.</p> <p>9 Q All right.</p> <p>10 MS. BROWN: Objection to the exercise.</p> <p>11 THE WITNESS: And I will say -- I mean I</p> <p>12 wasn't -- you know, that I don't necessarily --</p> <p>13 I'm not going to be able to necessarily agree or</p> <p>14 literally disagree with each one of these, but</p> <p>15 I'll just try to comment on what they -- what they</p> <p>16 have here and what it says to me.</p> <p>17 BY MS. PARFITT:</p> <p>18 Q All right. Well, why don't we take the</p> <p>19 first one.</p> <p>20 "Habitual use of talcum powder on the</p> <p>21 genital area may increase the risk for ovarian</p> <p>22 cancer, but the evidence is not strong."</p> <p>23 A Yeah.</p> <p>24 Q Do you agree with that?</p> <p>25 A I agree that the evidence is not strong.</p>
<p style="text-align: right;">Page 215</p> <p>1 -- the first sentence or the whole thing?</p> <p>2 Q The whole thing.</p> <p>3 A Yep. "A study at Harvard Medical School</p> <p>4 found that using talc this way doubled the risk,</p> <p>5 but other studies found no increased risk. Some</p> <p>6 researchers believe that talc may be carcinogenic</p> <p>7 because it contains particles of asbestos, a known</p> <p>8 carcinogen. It's been shown that rates of ovarian</p> <p>9 cancer are higher than normal in women whose jobs</p> <p>10 expose them to asbestos."</p> <p>11 Q All right. Thank you.</p> <p>12 Fair to say, Dr. Diette, that your</p> <p>13 opinions are contrary to the opinions of what --</p> <p>14 of those individuals at the Sidney Kimmel</p> <p>15 Comprehensive Cancer Center?</p> <p>16 MS. BROWN: Objection to the form of the</p> <p>17 question, lacks foundation.</p> <p>18 THE WITNESS: I wouldn't say globally.</p> <p>19 I mean there's -- there's things here that</p> <p>20 resonate with me just fine.</p> <p>21 BY MS. PARFITT:</p> <p>22 Q What resonates with you fine and what</p> <p>23 does not resonate with you?</p> <p>24 A Well, so, for example, when --</p> <p>25 Q And if you will, I'm going to put mine</p>	<p style="text-align: right;">Page 217</p> <p>1 And -- and I think it's a -- it's a pretty nuanced</p> <p>2 statement. It may increase, which leaves open</p> <p>3 that it may not increase. So I think it's a --</p> <p>4 it's a balanced statement. And their inclusion of</p> <p>5 the evidence not being strong is what resonates</p> <p>6 with me.</p> <p>7 Q Okay. Do you disagree, though, that</p> <p>8 it -- do you agree or disagree with this</p> <p>9 statement: "Habitual use of talcum powder on the</p> <p>10 genital area may increase the risk for ovarian</p> <p>11 cancer, but the evidence is not strong"?</p> <p>12 MR. LOCKE: Objection.</p> <p>13 BY MS. PARFITT:</p> <p>14 Q Do you agree with that statement?</p> <p>15 A I don't literally agree or disagree with</p> <p>16 it. I mean, I think I break it down the way that</p> <p>17 I did into those two parts.</p> <p>18 Q Okay. Well, I have a different</p> <p>19 question. I know how you want to do it, but I --</p> <p>20 I do get the ask the questions.</p> <p>21 MS. BROWN: He answered your question,</p> <p>22 Counsel.</p> <p>23 BY MS. PARFITT:</p> <p>24 Q Habitual question -- yes or no --</p> <p>25 MS. BROWN: No.</p>

Gregory B. Diette, M.D.

Page 218	Page 220
<p>1 BY MS. PARFITT: 2 Q "Habitual use of talcum powder on the 3 genital area may increase the risk for ovarian 4 cancer." True or false? 5 MR. LOCKE: Objection. 6 MS. BROWN: Objection to the form of the 7 question, asked and answered. 8 You can give the same answer again. 9 THE WITNESS: It's -- 10 MS. PARFITT: Counsel, please quit 11 instructing the witness. 12 MS. BROWN: Counsel, don't yell at me. 13 BY MS. PARFITT: 14 Q Go ahead. 15 MS. BROWN: We can call the Judge. 16 MS. PARFITT: I'm not yelling -- we can 17 call the Judge because I'll tell you, I don't 18 think he'll be -- she will be impressed. 19 MS. BROWN: That's fine. Let's go. 20 Let's walk right there and call her right now. 21 MS. PARFITT: I'm not going to waste the 22 time right now. 23 MS. BROWN: Okay. 24 THE WITNESS: So I don't see it as a 25 true or false questions. I think that there's two</p>	<p>1 than "may increase the risk," and it's very 2 different than saying it causes it. 3 BY MS. PARFITT: 4 Q Okay. 5 A So it's -- it's a pretty vague 6 statement. 7 Q Okay. And I think -- I hear what you're 8 saying, but my question, and I think you just 9 answered it, is if -- if Judge Wolfson says to 10 you, Dr. Diette, I would like an answer to my 11 question: Does the habitual use of talcum powder 12 on the genital area increase the risk for ovarian 13 cancer? 14 My -- my question to you from Judge 15 Wolfson. 16 MR. LOCKE: Objection. 17 MS. BROWN: Objection to the form of the 18 question, asked and answered. 19 THE WITNESS: And whether it does? 20 BY MS. PARFITT: 21 Q Yeah, the question is -- 22 A Well, it doesn't say that, though. 23 Q -- do you have -- no, no, no, I know it 24 doesn't. 25 A Oh.</p>
Page 219	Page 221
<p>1 parts, and I -- I like the way that I answered it. 2 BY MS. PARFITT: 3 Q Well, let me ask you this: My -- if 4 Judge Wolfson, who is the judge presiding over 5 this case, says to you, Dr. Diette, I've got a 6 question for you -- this is in July -- do you have 7 an opinion whether or not habitual use of talcum 8 powder on the genital area may increase the risk 9 for ovarian cancer, what are you going to tell 10 her? 11 MS. BROWN: Objection to the form of the 12 question and to the yelling at the witness. 13 BY MS. PARFITT: 14 Q I'm not yelling at you, Dr. Diette. 15 MS. PARFITT: Everyone is saying I 16 talk -- believe me, I'm not yelling at him. I'm 17 not that disrespectful. Trust me, please. 18 THE WITNESS: Okay. I don't think it 19 does, but, you know, there's so many ways you 20 could write this, which is why that it doesn't 21 strike me as something to agree or disagree with. 22 They could -- could have said "habitual use 23 causes." They could have said that it does 24 increase the risk. 25 So, you know, those are very different</p>	<p>1 Q I'm representing -- you've already told 2 me what you said about what's here. 3 A I see. 4 Q What I'm asking you is, do you have an 5 opinion whether or not the habitual use of talcum 6 powder -- powder on the genital area may increase 7 the risk for ovarian cancer? 8 A Not to quibble, but you just said does 9 increase before that, and now it's may increase? 10 Is it -- is it does increase -- 11 Q I'm going to do both, yeah. 12 A Okay. Well, I think this is so watered 13 down that it doesn't really say anything 14 definitive when you say "may increase." If the 15 question is about "does increase," I would say it 16 does not increase the risk. 17 Q Okay. And as worded, you feel that it's 18 somewhat equivocal. Is that fair? 19 MS. BROWN: Objection to the form of the 20 question. 21 THE WITNESS: Well, not the entire 22 statement. I mean the evidence is not strong. 23 Seems like a pretty -- a pretty potent part of the 24 statement. 25 BY MS. PARFITT:</p>

56 (Pages 218 to 221)

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 222</p> <p>1 Q Okay. So you agree with "the evidence 2 is not strong." 3 And then what about the next part, "A 4 study at Harvard Medical School found that using 5 talc this way doubled the risk, but other studies 6 found no increased risk." Do you agree with that 7 statement? 8 MS. BROWN: Objection to the form of the 9 question. 10 THE WITNESS: It's -- I would say maybe. 11 And the reason is because they -- they haven't 12 cited what the Harvard study is. It -- I could 13 assume, but I might be wrong that maybe it's the 14 Cramer study from '82. Maybe it's not. So I 15 don't know. So if they're citing that, then -- 16 then that might well be a correct statement. And 17 it's certainly correct that other studies have 18 found no increased risk. 19 BY MS. PARFITT: 20 Q All right. So from your review of the 21 medical and scientific literature, you have seen 22 where scientists who look at the same scientific 23 and medical literature can arrive at different 24 opinions, correct? 25 MS. BROWN: Objection to the form of the</p>	<p style="text-align: right;">Page 224</p> <p>1 MS. BROWN: -- of the question, 2 misstates the document, and it's been asked and 3 answered. 4 THE WITNESS: I'd be careful a lot of 5 ways, right? I think it's -- it's easy to say 6 what, you know, Johns Hopkins is saying. I don't 7 know how well this represents Johns Hopkins as an 8 entity. I -- like I don't know who controls this 9 website. I don't know who the author was. I 10 don't know if it was -- you know, somebody who was 11 hired for the summer to create a website or 12 whether it's somebody who is a credible 13 researcher. 14 But I also know that these kinds of 15 things populate all kinds of different websites, 16 and they're not necessarily like a policy 17 statement, you know, of a university or a hospital 18 or an entity. 19 BY MS. PARFITT: 20 Q And I'll -- 21 A I would just be careful, I mean just in 22 terms of saying Johns Hopkins is saying this. 23 Q Well, I will represent to you, and you 24 can see for yourself, that the Sidney Kimmel 25 Comprehensive Center puts out this information.</p>
<p style="text-align: right;">Page 223</p> <p>1 question. 2 THE WITNESS: Are we talking about a 3 specific topic or just you -- in general, that 4 scientists can disagree with each other? 5 BY MS. PARFITT: 6 Q Scientists can disagree with each other. 7 MS. BROWN: Objection to the form. 8 THE WITNESS: I think in general, they 9 can disagree about all sorts of things. I don't 10 think there's a good reason to disagree about this 11 topic that we're talking about. 12 BY MS. PARFITT: 13 Q Well, in this particular sentence, Johns 14 Hopkins University is representing to consumers, 15 or anyone who wants to get onto the website, that 16 medical schools found -- that a study of the 17 Harvard Medical School found that using talc this 18 way doubled the risk, but other studies found no 19 increased risk. 20 A Yes. 21 Q Is it fair to say they're communicating 22 that there are science -- there's science out 23 there that goes both ways? 24 MS. BROWN: Objection to the form -- 25 MR. LOCKE: Objection.</p>	<p style="text-align: right;">Page 225</p> <p>1 Your institution. 2 MS. BROWN: Objection to the form of the 3 question, and misstates the document. 4 THE WITNESS: It's the same issue. 5 Right. I mean I know the Sidney Kimmel Cancer 6 Center, and I work there. It's -- but I don't 7 know what the source is of this information, I 8 don't know who's the author, and I don't know what 9 they expect it to represent in terms of a Johns 10 Hopkins, you know, point of view. 11 BY MS. PARFITT: 12 Q Did anyone over at the Sidney Kimmel 13 Comprehensive Cancer Center ever consult you with 14 regard to what language should be included on the 15 website with regard to risk factor information? 16 A No. 17 MS. BROWN: Objection to the form. 18 BY MS. PARFITT: 19 Q Okay. The second part, let's go on. If 20 you will, it starts with -- if you can read on 21 "Some," if you would read that, please. 22 A "Some researchers believe that talc may 23 be carcinogenic because it contains particles of 24 asbestos, a known carcinogen." 25 Q All right. And do you agree with that</p>

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 226</p> <p>1 statement?</p> <p>2 MS. BROWN: Objection to the form.</p> <p>3 THE WITNESS: Well, I certainly agree</p> <p>4 that some researchers believe that, because we've</p> <p>5 seen it in plaintiffs' experts. So it's -- on its</p> <p>6 face, I think it's a -- a true -- true statement</p> <p>7 that there are people who believe that.</p> <p>8 And I think the part that asbestos is a</p> <p>9 known carcinogen is also something I agree with.</p> <p>10 BY MS. PARFITT:</p> <p>11 Q Okay. And then it goes on to say:</p> <p>12 "It's been shown that rates of ovarian cancer are</p> <p>13 higher than normal in women whose jobs expose them</p> <p>14 to asbestos."</p> <p>15 Do you agree with that statement?</p> <p>16 A So, you know, this language is -- is not</p> <p>17 great, right? It has been shown that, right. So</p> <p>18 we could look at, you know, any one of those</p> <p>19 studies that was done around World War II, for</p> <p>20 example, and if you looked at one that was</p> <p>21 positive, you could say it was shown that they</p> <p>22 were higher. I'm not sure whether the general</p> <p>23 proposition has been established, though.</p> <p>24 Q Okay.</p> <p>25 A If you guys are going to whisper, you're</p>	<p style="text-align: right;">Page 228</p> <p>1 out to the Food and Drug Administration to share</p> <p>2 your opinions with them?</p> <p>3 A No.</p> <p>4 Q All right. Other than counsel who has</p> <p>5 retained you to provide an expert -- a legal</p> <p>6 expert report, have you reached out to any</p> <p>7 scientific body to share your opinions?</p> <p>8 MS. BROWN: Objection to the form.</p> <p>9 THE WITNESS: No.</p> <p>10 BY MS. PARFITT:</p> <p>11 Q Okay. Have you reached out to any</p> <p>12 medical body to share your opinions?</p> <p>13 MS. BROWN: Objection to the form.</p> <p>14 THE WITNESS: No.</p> <p>15 BY MS. PARFITT:</p> <p>16 Q Okay. Did you reach out to the Sidney</p> <p>17 Kimmel Comprehensive Cancer Center and the folks</p> <p>18 over there and share with them what your opinions</p> <p>19 are?</p> <p>20 A No.</p> <p>21 MS. BROWN: Asked and answered.</p> <p>22 BY MS. PARFITT:</p> <p>23 Q Do you know Dr. Merlo?</p> <p>24 A I do.</p> <p>25 Q He's a friend of yours, right?</p>
<p style="text-align: right;">Page 227</p> <p>1 going to miss what I'm saying.</p> <p>2 Q No, I was -- I was just turned.</p> <p>3 A Okay.</p> <p>4 Q I heard what you said. Thank you.</p> <p>5 A All right.</p> <p>6 Q And fortunately, I have it right here in</p> <p>7 front of you too.</p> <p>8 A Okay, good. Good, good, good.</p> <p>9 Q Yeah, thank you. And I thought you had</p> <p>10 finished what you were saying because you finished</p> <p>11 "okay," so I thought --</p> <p>12 MS. BROWN: That's your "okay," Counsel.</p> <p>13 BY MS. PARFITT:</p> <p>14 Q I'm sorry. I believe you finished. I'm</p> <p>15 not sure whether the general proposition has been</p> <p>16 established. So I thought that was the end --</p> <p>17 A That was the end --</p> <p>18 Q -- of your sentence.</p> <p>19 A Yeah.</p> <p>20 Q Right. Okay. All right.</p> <p>21 A Are we done with this one?</p> <p>22 Q For the time being, yeah. We may come</p> <p>23 back to that.</p> <p>24 Other than providing counsel with an</p> <p>25 expert report of your opinions, have you reached</p>	<p style="text-align: right;">Page 229</p> <p>1 A He is.</p> <p>2 Q Okay. And you're Facebook friends.</p> <p>3 A I'm friends with his wife. He and I</p> <p>4 might be also, but we're friends in -- in reality,</p> <p>5 not just on --</p> <p>6 Q Not just on Facebook.</p> <p>7 A Yeah.</p> <p>8 Q Is his wife a doctor?</p> <p>9 A She is not.</p> <p>10 Q Okay. Do you know Dr. April</p> <p>11 Zambelli-Weiner?</p> <p>12 A I do.</p> <p>13 Q Okay. You have worked with her in the</p> <p>14 past, correct?</p> <p>15 A Really briefly, way back when.</p> <p>16 Q Okay. Do you consider her -- do you</p> <p>17 know she's an epidemiologist, correct?</p> <p>18 A I think I know that.</p> <p>19 Q Okay. Do you consider her an</p> <p>20 epidemiologist with expertise and well received in</p> <p>21 the medical comm- -- and scientific community?</p> <p>22 MS. BROWN: Objection. Lacks</p> <p>23 foundation, calls for speculation.</p> <p>24 THE WITNESS: So I don't know much</p> <p>25 about -- about her lately. I think the last time</p>

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 230</p> <p>1 that I saw her was when she was still training at 2 Hopkins. And so there's a couple of decades that 3 have gone by. So I -- so I honestly have no idea 4 what her reputation is at this point. 5 BY MS. PARFITT: 6 Q Okay. Did you work with her? 7 A Sort of. Like not -- we were -- we were 8 both involved in a research project, but we 9 weren't both involved in the same part of the 10 project. So I -- it's -- to say that we worked 11 together, it's -- it's a little bit vague in a way 12 about whether we did. We traveled together for 13 one particular research program we were a part of. 14 But -- 15 Q Okay. 16 A Like I don't think we published 17 together. I don't think. 18 Q Do you think of her as a good scientist? 19 MS. BROWN: Objection to the form of the 20 question, calls for speculation. 21 THE WITNESS: I -- I honestly don't know 22 what she's -- what she's up to. I mean it's 23 literally been a couple of decades. 24 BY MS. PARFITT: 25 Q Sure. Well, when you did know her back</p>	<p style="text-align: right;">Page 232</p> <p>1 appear and give testimony, correct? 2 A Correct. 3 MS. BROWN: Form. 4 BY MS. PARFITT: 5 Q Right. So no one inquired as to what 6 your opinions were on this topic; is that correct? 7 MS. BROWN: Asked and answered. 8 THE WITNESS: That is correct. 9 BY MS. PARFITT: 10 Q Okay. I'll represent to you that at the 11 hearing, both consumer and industry were invited 12 to attend. 13 Are you aware that Dr. McTiernan, who is 14 an expert in this case, was one of those 15 individuals that was invited to attend? 16 MR. LOCKE: Objection. 17 MS. BROWN: Objection. Lacks 18 foundation. 19 THE WITNESS: I don't know. 20 BY MS. PARFITT: 21 Q Okay. You've read her expert report, 22 correct? 23 A I did. 24 Q And you understand that she was one of 25 the coinvestigators with the WHI study?</p>
<p style="text-align: right;">Page 231</p> <p>1 a couple of decades ago, did you consider her a 2 good scientist? 3 MS. BROWN: Objection to the form, 4 vague, calls for speculation. 5 THE WITNESS: I wouldn't say that I know 6 that she wasn't, but I really wasn't very familiar 7 with what her work was. 8 BY MS. PARFITT: 9 Q Her work. Okay. That's fair enough. 10 Okay. Alrighty. Let's set this aside. 11 Dr. Diette, are you aware that just last 12 month, and I believe it was March 12th, the House 13 Committee on Oversight and Reform, Committee on 14 Economic and Consumer Policy conducted a hearing 15 about the public health risk of carcinogens in 16 talcum powder products and other consumer 17 products? Were you aware of that? 18 MR. LOCKE: Objection. 19 MS. BROWN: Objection to the form. 20 THE WITNESS: I saw that -- a question 21 about that in one of the deposition transcripts 22 that I -- that I read. I don't remember which 23 one. But that's my only awareness of that. 24 BY MS. PARFITT: 25 Q Okay. So no one requested that you</p>	<p style="text-align: right;">Page 233</p> <p>1 MS. BROWN: Objection to the form. 2 BY MS. PARFITT: 3 Q One of the cohorts that you rely on. 4 MS. BROWN: Foundation, speculation. 5 THE WITNESS: That's what I understand. 6 BY MS. PARFITT: 7 Q Okay. When you were writing your expert 8 report and researching the cohort studies, did you 9 ever reach out to Dr. McTiernan to consult with 10 her with regard to her thoughts and opinions about 11 that particular cohort study? 12 MS. BROWN: Objection to the form. 13 Which study? 14 MS. PARFITT: I said the WHI study. 15 MS. BROWN: It's not in your question. 16 THE WITNESS: Assuming the WHI study, I 17 did not. 18 BY MS. PARFITT: 19 Q Okay. Dr. McTiernan testified at that 20 hearing, and her testimony went uncontroverted, 21 that there was a statistically significant 22 increased risk of 22 to 31 percent of developing 23 ovarian cancer from genital use of talcum powder 24 products. 25 Do you agree or disagree with that?</p>

Gregory B. Diette, M.D.

Page 234	Page 236
<p>1 MR. LOCKE: Objection.</p> <p>2 MS. BROWN: Objection. This lacks</p> <p>3 foundation. Counsel, are you giving him a</p> <p>4 hypothetical? Or if not, are you going to give</p> <p>5 him something that would support the statements</p> <p>6 that you're making on the record?</p> <p>7 BY MS. PARFITT:</p> <p>8 Q Assume that Dr. McTiernan testified</p> <p>9 before the subcommittee who was investigating the</p> <p>10 safety of talcum powder products, that</p> <p>11 Dr. McTiernan testified that there was scientific</p> <p>12 evidence that women who used talcum powder</p> <p>13 products have a statistically significant</p> <p>14 increased risk of 22 to 31 percent of developing</p> <p>15 ovarian cancer.</p> <p>16 A So, first of all --</p> <p>17 MS. BROWN: Wait, wait. What's the</p> <p>18 question?</p> <p>19 BY MS. PARFITT:</p> <p>20 Q And I should add developing epithelial</p> <p>21 ovarian cancer having used talcum powder products.</p> <p>22 MS. BROWN: What's the question? You</p> <p>23 just gave an assumption.</p> <p>24 BY MS. PARFITT:</p> <p>25 Q Do you --</p>	<p>1 March 12th, 2019.</p> <p>2 Do you see that?</p> <p>3 A I see it.</p> <p>4 Q Okay. If I can direct your attention</p> <p>5 to -- and I'll represent that this was a statement</p> <p>6 that she submitted prior to the hearing, and</p> <p>7 specifically -- I can put it on the ELMO here.</p> <p>8 Let's go down to the third full paragraph.</p> <p>9 Do you see that, it starts</p> <p>10 "Summarizing"?</p> <p>11 A Yes.</p> <p>12 Q Okay. And it states: "Summarizing data</p> <p>13 from all of the published studies consistently</p> <p>14 shows that women who had ever used talcum powder</p> <p>15 products in the genital area had a statistically</p> <p>16 significant 22 to 31 percent increased risk of</p> <p>17 developing epithelial ovarian cancer compared with</p> <p>18 women who had never used them. Evidence suggests</p> <p>19 that these associations hold across diverse race</p> <p>20 and ethnic groups."</p> <p>21 Did I read that correctly?</p> <p>22 A You did.</p> <p>23 Q All right. Do you agree with that</p> <p>24 statement?</p> <p>25 MS. BROWN: Objection to the form.</p>
Page 235	Page 237
<p>1 MS. PARFITT: I just was finishing.</p> <p>2 BY MS. PARFITT:</p> <p>3 Q But do you agree with her statement</p> <p>4 before Congress?</p> <p>5 MS. BROWN: Objection to the form.</p> <p>6 MR. LOCKE: Objection.</p> <p>7 MS. BROWN: Incomplete hypothetical,</p> <p>8 lacks foundation, calls for speculation.</p> <p>9 THE WITNESS: So I don't know what she</p> <p>10 said -- and I know you're asking me to assume what</p> <p>11 she said -- I don't know what else she said about</p> <p>12 it, so how the -- how that's framed -- it sounds</p> <p>13 compatible generally with what her report had at</p> <p>14 least one sentence about.</p> <p>15 BY MS. PARFITT:</p> <p>16 Q Okay. Let me show you what we'll have</p> <p>17 marked as Exhibit 13.</p> <p>18 (Diette Exhibit No. 13 was marked</p> <p>19 for identification.)</p> <p>20 BY MS. PARFITT:</p> <p>21 Q And I'll represent to you that this</p> <p>22 is the statement of Ann McTiernan that was</p> <p>23 prepared for the Subcommittee on Economic and</p> <p>24 Consumer Policy on "Examining the Public Health</p> <p>25 Risks of Carcinogens in Consumer Products" dated</p>	<p>1 THE WITNESS: Well, I think this is</p> <p>2 compatible with what, you know, her report and her</p> <p>3 testimony has been generally. I think it's --</p> <p>4 it's -- unfortunately, it's not very balanced,</p> <p>5 right. I mean she -- she's leaving out an awful</p> <p>6 lot of information here and -- and really</p> <p>7 referring just to one narrow slice of the evidence</p> <p>8 that she's -- that she's citing here.</p> <p>9 BY MS. PARFITT:</p> <p>10 Q Okay. What did she leave out, Doctor?</p> <p>11 A I'm sorry?</p> <p>12 Q What is she leaving out?</p> <p>13 A Well, saying that -- that "data from all</p> <p>14 the published studies consistently shows that</p> <p>15 women who had ever used talcum powder products in</p> <p>16 the genital area had a statistically significant</p> <p>17 22 to 31 percent increased risk," and I won't</p> <p>18 finish the rest, but, you know, of developing</p> <p>19 ovarian cancer.</p> <p>20 So, you know, they don't all have a</p> <p>21 statistically significant increase, and she's</p> <p>22 leaving out information that would run counter to</p> <p>23 that also, including I think -- let me just see</p> <p>24 what she cites.</p> <p>25 She cites Berge and Penninkilampi and</p>

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 238</p> <p>1 Terry, but there's other information in there, 2 like from Berge, for example, you know, who points 3 out that there's no risk seen in the cohort 4 studies. So I think if this were balanced, that 5 she would -- she would have more information than 6 just that particular statement. 7 Q Okay. And we'll talk a little bit more 8 about the -- the cohorts in just -- just a moment. 9 Okay. What was the methodology you 10 employed in order to present the opinions and 11 bases for opinions in your report? 12 A So generally, I tried to identify all of 13 the relevant epidemiologic studies -- is that what 14 you're -- you're asking? 15 Q That is? 16 A Okay. 17 Q That is. 18 A And so I tried to find them in an 19 iterative way, you know, meaning that there were 20 meta-analyses that had many of them listed. I did 21 some searches of their own reference lists to look 22 for others. I did searches, you know, using 23 web-based, you know, tools to find other -- other 24 studies, and tried to get what I thought was a 25 pretty comprehensive group of all the</p>	<p style="text-align: right;">Page 240</p> <p>1 search terms that you used in order to do your 2 literature review? 3 A I didn't -- I didn't write them down, 4 but it -- you know, this didn't start as like a -- 5 like a -- like there's been some searches that 6 I've been involved in where, you know, somebody 7 might commission a review of a particular topic, 8 and you have to figure out what those search terms 9 are. 10 In this case, there's a really good head 11 start because there's meta-analyses done and 12 there's some other -- some other papers. And so 13 what I tried to use was the words that the authors 14 used, you know, assuming that they would then link 15 up and find the other -- other articles. 16 So -- so like "ovarian cancer," "talc," 17 "talcum powder," probably some -- you know, some 18 words like "risk" and "cause" and -- I think for 19 that part of it that was -- that was kind of the 20 bulk of it. There may have been other terms that 21 came up in some of the -- some of the articles 22 that I would search for also, but that -- that was 23 the main ones. 24 Q Did you search for the word "cancer"? 25 A Oh, well, "ovarian cancer."</p>
<p style="text-align: right;">Page 239</p> <p>1 epidemiologic studies. 2 And then I also tried to read other 3 things, you know, IARC monographs, other -- like 4 reports from like American College of Obstetrics 5 and Gynecology, and -- and get a sense of how some 6 of the information was being interpreted by 7 other -- other bodies. 8 And -- and then ultimately looked at 9 criteria that people recognize as useful for 10 assessing causation, which are labeled sometimes 11 Bradford Hill considerations, and then other 12 things too. 13 So besides that, then, you know, looking 14 at the quality of the studies in some cases. So, 15 for example, were there valid measures of -- of 16 exposure that were used, was there evidence for 17 confounding and bias, and so forth. 18 Q All right. 19 A Meaning especially those latters 20 aren't -- those latter factors aren't part of 21 Bradford Hill. Like he doesn't talk about, you 22 know, bias and confounding and validity of the 23 measures and so forth. So there's more to looking 24 at it than just Bradford Hill. 25 Q Okay. So what was -- what were the</p>	<p style="text-align: right;">Page 241</p> <p>1 Q Okay. Did you search for the word 2 "asbestos"? 3 A I did, but differently -- so I did sort 4 of a separate search for that, which was "asbestos 5 and ovarian cancer." Same approach, but -- but 6 different -- I thought we were just talking about 7 the talcum powder at the moment. 8 But separately, I did a search for 9 "asbestos and -- and ovarian cancer." And -- and 10 just like for this issue of talcum powder, there 11 was a good head start from -- from IARC, at least 12 having identified several -- several key studies, 13 and then looked for more because there were 14 obviously some that they didn't cite or that 15 weren't available to them at the time that they 16 did their -- their review. 17 Q Did you search for the word 18 "inflammation"? 19 A I did, for -- part of the searches was 20 for inflammation. 21 Q Okay. 22 A I should say also -- I mean there's more 23 to it if you want, just a little bit more. 24 Q No. Let me ask you a question first. 25 A Okay.</p>

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 242</p> <p>1 Q There's no question pending.</p> <p>2 I assume you did a literature search</p> <p>3 back in the early part of 2017 when you were first</p> <p>4 retained, correct?</p> <p>5 A Correct.</p> <p>6 Q All right. So did you update that</p> <p>7 literature search?</p> <p>8 A Oh, yeah.</p> <p>9 Q Okay. Did you keep -- do you keep some</p> <p>10 kind of recordation of material you had before and</p> <p>11 then what material you're looking at now for</p> <p>12 purposes of this most recent report?</p> <p>13 A No, I mean it's not sorted by -- by when</p> <p>14 I found it.</p> <p>15 Q All right. You represented, at least in</p> <p>16 your report, that you looked at the databases</p> <p>17 Medline and Google.</p> <p>18 Did you use any other databases for your</p> <p>19 research?</p> <p>20 A Well, scholar -- Google Scholar as</p> <p>21 opposed to just plain Google and then main Google</p> <p>22 itself. I don't remember if I used any others.</p> <p>23 Q Okay. Where in your report do you share</p> <p>24 your systematic review and collection of the</p> <p>25 various literature that formed the bases of your</p>	<p style="text-align: right;">Page 244</p> <p>1 A Some --</p> <p>2 MS. BROWN: Objection to the form.</p> <p>3 THE WITNESS: Some of it.</p> <p>4 BY MS. PARFITT:</p> <p>5 Q Okay. And how did you select the</p> <p>6 case -- the cases that became part of your list of</p> <p>7 cases on page 13 and 14 of your report?</p> <p>8 A What does "cases" mean?</p> <p>9 Q Studies. You have them listed on</p> <p>10 page 13, and it carries over to page 14.</p> <p>11 A It's -- the way I describe it, I don't</p> <p>12 think I got to finish answering the question about</p> <p>13 the -- the rest of the methodology. You'd have to</p> <p>14 turn over to page 6, and in the section called</p> <p>15 "Review of Epidemiology Data," there's a</p> <p>16 description of what I just told you verbally just</p> <p>17 a moment ago, which is talking about MedLine and</p> <p>18 Google Scholar, and reviewed the reference list of</p> <p>19 the individual studies and the meta-analyses to</p> <p>20 assemble a complete list of studies, and then I --</p> <p>21 it goes on. That's not the whole paragraph</p> <p>22 obviously, but that's the -- that's the general</p> <p>23 method of how I found them.</p> <p>24 Q Okay. And what process did you go</p> <p>25 through to select or deselect certain pieces of</p>
<p style="text-align: right;">Page 243</p> <p>1 opinion?</p> <p>2 A I didn't write that part, I don't think,</p> <p>3 but it -- I do talk about the -- the methodology</p> <p>4 in general.</p> <p>5 Q Okay. Well, you talk about the</p> <p>6 methodology on page -- I believe it's page 4, and</p> <p>7 there's about two paragraphs there, and then on</p> <p>8 the top of page 5, where there's just two full</p> <p>9 paragraphs.</p> <p>10 So my question is, where do you -- is</p> <p>11 there anywhere else in your report that you set</p> <p>12 forth your methodology --</p> <p>13 A Yeah.</p> <p>14 Q -- employed in order to --</p> <p>15 A Sure, other places --</p> <p>16 Q -- form the basis for your opinions?</p> <p>17 A Sorry, I didn't mean to interrupt.</p> <p>18 Q No, and what I'm saying --</p> <p>19 A Were you done?</p> <p>20 Q -- you have a methodology section --</p> <p>21 let's start over.</p> <p>22 You have a methodology section of your</p> <p>23 report. Is it fair that that is where you set</p> <p>24 forth the methodology that you employ in this</p> <p>25 case?</p>	<p style="text-align: right;">Page 245</p> <p>1 literature that you reviewed?</p> <p>2 A Well, I -- I included all of the ones</p> <p>3 that I could find. I mean we're talking about the</p> <p>4 epidemiologic studies.</p> <p>5 Q We are. We are indeed, yeah.</p> <p>6 A So like in terms of the cohort studies,</p> <p>7 there's only three I could find. There's more</p> <p>8 than three publications that pertain to the three,</p> <p>9 but I included all three, and I included all the</p> <p>10 publications I could find on the topic.</p> <p>11 But the case-control study, a similar</p> <p>12 approach, although there's a little bit of</p> <p>13 confusion with the case controls because there's</p> <p>14 overlap. There is a redundant publication where</p> <p>15 some authors are presenting the same data twice,</p> <p>16 and it's not entirely clear how to unravel them.</p> <p>17 So I just tried to include as many of those as I</p> <p>18 could that looked like distinct studies, and I</p> <p>19 tried to make sure I had the -- you know, the vast</p> <p>20 majority of what was being considered in the</p> <p>21 meta-analysis as well.</p> <p>22 Q I think where I'm going is, where do</p> <p>23 you -- where do you tell the -- the reader what</p> <p>24 your inclusion criteria was for selecting studies?</p> <p>25 MS. BROWN: Objection to the form.</p>

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 246</p> <p>1 THE WITNESS: I tried to get them all. 2 I wasn't trying to exclude any studies. 3 BY MS. PARFITT: 4 Q So every -- so may I assume from that 5 statement that all of the literature that you've 6 listed on page 13 and 14 in the cohort studies and 7 the meta-analysis is the entire body of literature 8 that you reviewed? 9 A Of course not. 10 MS. BROWN: Objection to the form. 11 THE WITNESS: No, no, what -- well, I 12 guess, if you could, please be very precise what 13 you're asking. 14 To me what I think we're talking about 15 is the case-control studies and the cohort 16 studies, and so I tried to identify every single 17 one of them. So I didn't have an exclusion 18 criteria to say I was going to ignore this one 19 because it wasn't supportive of my view or 20 something like that. I included them all. 21 I searched for clinical trials, but 22 there weren't any. So that was -- that was an 23 issue as well. 24 BY MS. PARFITT: 25 Q Were there any studies that you chose</p>	<p style="text-align: right;">Page 248</p> <p>1 of the risk -- risk estimates, not of the number 2 of cases. 3 BY MS. PARFITT: 4 Q Correct. So where on this page 13 or 14 5 do you tell the reader how many ovarian cancer 6 cases were part of that study? 7 MS. BROWN: Objection to the form. 8 THE WITNESS: It's not on there. 9 BY MS. PARFITT: 10 Q Okay. Where on your list of cases, 13 11 and 14, do you tell the reader the number of 12 controls that were involved in that study? 13 A I didn't -- I didn't list every single 14 thing like that on here. 15 Q You didn't list it in your report 16 either, correct? 17 MS. BROWN: Objection to the form. 18 THE WITNESS: Well, this is the report. 19 BY MS. PARFITT: 20 Q Well, you didn't list it anywhere else 21 other -- that information is not contained in your 22 report. Is that fair? 23 MS. BROWN: Objection to the form. 24 MR. LOCKE: Objection. 25 THE WITNESS: The sample size?</p>
<p style="text-align: right;">Page 247</p> <p>1 not to include on your list of 13 and 14 that you 2 had actually reviewed during the course of your 3 study? 4 A And we're talking about case-control 5 studies and cohorts. 6 Q Correct. 7 A I didn't -- wait a minute. I didn't 8 deliberately not include any of them. I tried to 9 include every single one, with that exception 10 being -- and I don't remember which ones were 11 which, but there were a couple that were 12 redundant. You know, the -- the authors of these 13 haven't in every case been careful about reporting 14 findings that are unique. 15 Q Okay. Focusing now, if I may, on your 16 chart, page 13 and 14 of the case-control studies. 17 Do you have that in front of you? 18 A Almost. 19 Q Okay. 20 A I do. 21 Q All right. Where in this document, 22 page 13 and 14, do you identify the number of 23 ovarian cases that formed the bases of the study? 24 MS. BROWN: Objection to the form. 25 THE WITNESS: This is the list of the --</p>	<p style="text-align: right;">Page 249</p> <p>1 BY MS. PARFITT: 2 Q The sample size is not information that 3 you contained -- that you included in your report, 4 correct? 5 A I did not. 6 MS. BROWN: Same objection. 7 BY MS. PARFITT: 8 Q Okay. Where in your report do you tell 9 the reader the country from where these studies 10 came from? 11 MS. BROWN: Objection to the form. 12 THE WITNESS: I don't list that. 13 BY MS. PARFITT: 14 Q Okay. Where do you tell the reader what 15 the mean age of the participants in this study 16 were? 17 MS. BROWN: Same objection. 18 THE WITNESS: And same answer, I 19 don't -- I don't list that either. 20 BY MS. PARFITT: 21 Q Where in your report do you tell the 22 reader the number of adjusted variables per study 23 that were considered? 24 MS. BROWN: Objection to the form. 25 THE WITNESS: I didn't -- I didn't</p>

Gregory B. Diette, M.D.

Page 250	Page 252
<p>1 capture that here.</p> <p>2 BY MS. PARFITT:</p> <p>3 Q Okay. And where in your report do you</p> <p>4 tell the reader the type of ovarian cancer that</p> <p>5 the women suffered?</p> <p>6 MS. BROWN: Objection to the form.</p> <p>7 THE WITNESS: That's not listed on -- on</p> <p>8 this table either.</p> <p>9 BY MS. PARFITT:</p> <p>10 Q Did you create this table yourself or</p> <p>11 did you have assistance?</p> <p>12 A So, actually, I made this initially, and</p> <p>13 there might have been a couple that filtered in</p> <p>14 after I started to create it where -- you know,</p> <p>15 where I had an assistant, you know, plug in a</p> <p>16 different study.</p> <p>17 Q Where in your report do you tell the</p> <p>18 reader if you applied a scoring system to the data</p> <p>19 and the studies that you reviewed?</p> <p>20 A That wasn't --</p> <p>21 MS. BROWN: Objection. Lacks</p> <p>22 foundation.</p> <p>23 THE WITNESS: That wasn't my approach.</p> <p>24 BY MS. PARFITT:</p> <p>25 Q Okay. We'll talk about that in a</p>	<p>1 Q What specific, if any, in vitro studies</p> <p>2 did you consider for purposes of your opinion?</p> <p>3 A So I -- are you good?</p> <p>4 Q Yeah, thank you.</p> <p>5 A Okay. So I -- I don't know if you're</p> <p>6 including some animal studies as in vitro studies</p> <p>7 or whether you just mean sort of like ones that</p> <p>8 are -- that are cell-based or in a dish.</p> <p>9 Q Well, there's a difference, isn't there?</p> <p>10 A There should be, yeah, but I just --</p> <p>11 since you're asking the question, I don't know</p> <p>12 you, and so I -- I just want to be clear.</p> <p>13 Q No, I'm -- I'm cognizant of the</p> <p>14 difference between in vivo and in vitro, so what</p> <p>15 I -- what I would ask you is what in vitro studies</p> <p>16 did you consider for purposes of your analysis?</p> <p>17 A Yeah, I looked at some. I think the</p> <p>18 ones that were cited by IARC I looked at. I don't</p> <p>19 remember the full list of ones -- which ones I may</p> <p>20 have listed, if any, that -- that I looked at.</p> <p>21 But that wasn't really my main -- my main purpose</p> <p>22 in looking at the epidemiology, which was to --</p> <p>23 was to look at in vitro studies.</p> <p>24 Q Okay. Was part of your analysis -- or</p> <p>25 did part of your analysis include looking at</p>
Page 251	Page 253
<p>1 minute. Appreciate that.</p> <p>2 Did you exercise any independent</p> <p>3 judgment in determining what cases to include on</p> <p>4 this chart of case-control studies on 13 and 14?</p> <p>5 MS. BROWN: Objection. Asked and</p> <p>6 answered.</p> <p>7 THE WITNESS: I tried to be inclusive.</p> <p>8 BY MS. PARFITT:</p> <p>9 Q Being inclusive -- did being inclusive</p> <p>10 require you to exercise professional judgment with</p> <p>11 regard to selection of the cases that you reviewed</p> <p>12 and included for purposes of your analysis?</p> <p>13 A So, mostly, yes. What I would say is I</p> <p>14 was trying to understand what the universe was of</p> <p>15 case controls that were being listed in the</p> <p>16 meta-analyses, what the case controls were that</p> <p>17 were informing the opinions of the plaintiffs'</p> <p>18 experts. And so I didn't want to have some</p> <p>19 arbitrary rule for saying one shouldn't be in</p> <p>20 here. I wanted to look at them all. And so my</p> <p>21 goal was actually to include them all, and not</p> <p>22 deselect some because I thought that there was a</p> <p>23 quality issue with them.</p> <p>24 (Brief interruption.)</p> <p>25 BY MS. PARFITT:</p>	<p>1 in vivo studies?</p> <p>2 A So I looked at -- at a bunch of the</p> <p>3 different animal studies that were cited, cited in</p> <p>4 some of the other documents.</p> <p>5 Q Which ones?</p> <p>6 A So I don't remember the author names. I</p> <p>7 mean, there were -- there were studies of, you</p> <p>8 know, rats, rabbits, primates. I can't remember</p> <p>9 if there were mouse -- there were mouse studies as</p> <p>10 well.</p> <p>11 So whatever that list is that was in</p> <p>12 IARC that they had considered at that point, and</p> <p>13 then I think I found a couple more.</p> <p>14 Q What, if any, information did you glean</p> <p>15 from your review of the in vitro and in vivo</p> <p>16 studies that formed the basis of your study</p> <p>17 report?</p> <p>18 A Well, mostly -- so to -- to think about</p> <p>19 how -- for me as an epidemiologist, and not as a</p> <p>20 cancer biologist or molecular biologist, I wanted</p> <p>21 to just understand generally how some of the other</p> <p>22 entities were wielding that information, right.</p> <p>23 So that -- like I wasn't about to become a cancer</p> <p>24 biologist in reading these things or understand</p> <p>25 whether their methods were appropriate or not, but</p>

64 (Pages 250 to 253)

Gregory B. Diette, M.D.

Page 254	Page 256
<p>1 I did want to understand some of their</p> <p>2 underpinnings.</p> <p>3 Q Okay.</p> <p>4 A And just so, for example, right, so</p> <p>5 there's the -- the studies on migration, for</p> <p>6 example. I thought it was important to look at</p> <p>7 those and see what kind of animals, for example,</p> <p>8 had what kind of particles either put into their</p> <p>9 vaginas or put into their uterus, or whatever it</p> <p>10 was, so I could understand what the -- what the</p> <p>11 story was there.</p> <p>12 Q Okay. Do animals have vaginas?</p> <p>13 A Some do, yeah.</p> <p>14 Q You -- you indicated you're not a cancer</p> <p>15 specialist. Would you defer to -- on topics</p> <p>16 involving those issues to a cancer biologist?</p> <p>17 MS. BROWN: Objection to the form of the</p> <p>18 question.</p> <p>19 BY MS. PARFITT:</p> <p>20 Q And let me clean it up because I think I</p> <p>21 left that off. You are not a cancer biologist,</p> <p>22 correct?</p> <p>23 A Correct.</p> <p>24 Q All right. So would you defer questions</p> <p>25 in that wheelhouse to someone who is a cancer</p>	<p>1 MS. BROWN: What report is --</p> <p>2 MS. PARFITT: Saed.</p> <p>3 BY MS. PARFITT:</p> <p>4 Q Just give me a moment, Doctor.</p> <p>5 If you turn your attention to page 42.</p> <p>6 A Mm-hmm.</p> <p>7 Q At the bottom.</p> <p>8 A Okay.</p> <p>9 Q "I leave a detailed assessment of</p> <p>10 Dr. Saed's efforts to other experts. I did review</p> <p>11 Dr. Saed's report and his two depositions and was</p> <p>12 struck by the irregularities in his study, which</p> <p>13 render his results highly questionable."</p> <p>14 So are you or are you not deferring with</p> <p>15 regard to opinions concerning what Dr. Saed had to</p> <p>16 say?</p> <p>17 MS. BROWN: Objection. Misstates the</p> <p>18 expert report and the opinion.</p> <p>19 THE WITNESS: I -- I meant to be</p> <p>20 somewhat nuanced here, right, which is that -- you</p> <p>21 know, it's possible for me to read things and</p> <p>22 understand that there might be some issues with</p> <p>23 what he's done. I -- I'm not going to be the</p> <p>24 person to critique the biologic aspects of his</p> <p>25 work, though.</p>
Page 255	Page 257
<p>1 biologist?</p> <p>2 MS. BROWN: Same objection.</p> <p>3 THE WITNESS: So I mostly don't think</p> <p>4 about deferring my opinions to other -- other</p> <p>5 people's categorically. You know, so that I think</p> <p>6 if there were somebody that was a cancer biologist</p> <p>7 and they had an opinion that seemed credible, I</p> <p>8 would take it into account. But to the extent</p> <p>9 that I needed to understand something, I would</p> <p>10 still rely on my own -- my own background and</p> <p>11 knowledge.</p> <p>12 BY MS. PARFITT:</p> <p>13 Q All right. You're not a -- a molecular</p> <p>14 specialist, correct?</p> <p>15 MS. BROWN: Objection.</p> <p>16 THE WITNESS: Not a molecular biologist.</p> <p>17 BY MS. PARFITT:</p> <p>18 Q Okay. I believe you stated in your</p> <p>19 report that you were deferring to other experts in</p> <p>20 this case as it pertains to the opinions that</p> <p>21 Dr. Saed has given; is that correct?</p> <p>22 MS. BROWN: Objection to the form.</p> <p>23 Counsel, is there a part of the report you're</p> <p>24 referring to?</p> <p>25 MS. PARFITT: Mm-hmm, there is.</p>	<p>1 BY MS. PARFITT:</p> <p>2 Q Okay. Fair enough. In fact, let me ask</p> <p>3 you, have you read the published scientific</p> <p>4 article by Dr. Saed?</p> <p>5 A Not yet.</p> <p>6 Q Okay. Do you have any plans to do that?</p> <p>7 A I might. I might, because I was just --</p> <p>8 I was curious because I saw some of the -- like</p> <p>9 the expert reports that came in after I wrote my</p> <p>10 report, and there were things that just kind of</p> <p>11 struck me that would be worth trying to sort</p> <p>12 through, like whether he had changed like 48 to 36</p> <p>13 or -- yeah, 48 hours to 72 hours, whatever it was,</p> <p>14 that there were like some tables apparently that</p> <p>15 were the same as an original paper, that the only</p> <p>16 change was like the numbers on them. And so just</p> <p>17 to sort of understand the quality issues related</p> <p>18 to the study, I thought I might take a look at it.</p> <p>19 Q All right. But prior to preparing your</p> <p>20 expert report, and, frankly, this deposition</p> <p>21 today, you have not read either Dr. Saed's -- you</p> <p>22 have not read Dr. Saed's most current peer-</p> <p>23 reviewed paper, correct?</p> <p>24 A True for both time periods. I don't</p> <p>25 think it was published or available to me before I</p>

65 (Pages 254 to 257)

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 258</p> <p>1 did the report, but I could be wrong.</p> <p>2 Q Well, it's available now, isn't it?</p> <p>3 A That's what I've heard.</p> <p>4 MS. BROWN: Objection to the form.</p> <p>5 BY MS. PARFITT:</p> <p>6 Q But you've not seen it.</p> <p>7 A No. I just -- I mean like -- I mean</p> <p>8 it -- sorry, it's the way I think. It sounds like</p> <p>9 two different time periods. One was --</p> <p>10 Q No.</p> <p>11 A -- before the report and one was between</p> <p>12 then and now.</p> <p>13 Q No, my question goes --</p> <p>14 MS. BROWN: Wait, he's finishing. Let</p> <p>15 him finish.</p> <p>16 BY MS. PARFITT:</p> <p>17 Q My question -- are you done?</p> <p>18 A I'm good.</p> <p>19 Q My question really goes to, is it fair</p> <p>20 to say that you have not read Dr. Saed's published</p> <p>21 peer-reviewed article at the time of your</p> <p>22 deposition?</p> <p>23 A That is correct.</p> <p>24 THE WITNESS: Sorry.</p> <p>25 MS. BROWN: That's all right.</p>	<p style="text-align: right;">Page 260</p> <p>1 think, but I've certainly read other -- I mean</p> <p>2 others that aren't on either of those topics.</p> <p>3 Q Would you agree -- would you agree that</p> <p>4 IARC is a well-respected scientific organization?</p> <p>5 MS. BROWN: Object -- I'm sorry. I</p> <p>6 didn't hear the question.</p> <p>7 BY MS. PARFITT:</p> <p>8 Q Would you agree that IARC is a well-</p> <p>9 respected scientific organization?</p> <p>10 MS. BROWN: Objection to the form.</p> <p>11 THE WITNESS: It's -- it's hard for me</p> <p>12 to characterize whole organizations, you know, in</p> <p>13 terms of whether they're well respected or by whom</p> <p>14 or when, but generally speaking, you know, they --</p> <p>15 they do produce some -- some credible documents.</p> <p>16 BY MS. PARFITT:</p> <p>17 Q They do produce some credible documents.</p> <p>18 It's -- IARC is part of the World Health</p> <p>19 Organization, correct?</p> <p>20 A It is.</p> <p>21 Q Okay. And when IARC has its meetings to</p> <p>22 discuss classification of carcinogens, it invites</p> <p>23 world-renowned experts for whatever area and</p> <p>24 specialty is being discussed. Is that fair?</p> <p>25 MS. BROWN: Objection to the form.</p>
<p style="text-align: right;">Page 259</p> <p>1 BY MS. PARFITT:</p> <p>2 Q Okay. Now, you've mentioned IARC a</p> <p>3 couple of times during the course of your</p> <p>4 testimony.</p> <p>5 Have you rereviewed the IARC</p> <p>6 monographs -- or the IARC monogram that was</p> <p>7 published in 2010 on silica?</p> <p>8 MS. BROWN: The monograph?</p> <p>9 MS. PARFITT: The monograph. Monograph.</p> <p>10 MS. BROWN: Monograph on talc?</p> <p>11 MS. PARFITT: On talc, mm-hmm.</p> <p>12 THE WITNESS: Did you just say silica or</p> <p>13 no?</p> <p>14 BY MS. PARFITT:</p> <p>15 Q I did say silica. I meant talc.</p> <p>16 A You meant talc. Yeah, I've read the</p> <p>17 talc one.</p> <p>18 Q You've read the talc one. Have you read</p> <p>19 the 2012 monograph, the one 100C, have you seen</p> <p>20 that?</p> <p>21 A I have.</p> <p>22 Q Okay. Have you read any other</p> <p>23 monographs on talc or asbestos?</p> <p>24 A I've read earlier ones on asbestos. I</p> <p>25 don't know of any other ones on talc, I don't</p>	<p style="text-align: right;">Page 261</p> <p>1 MR. LOCKE: Objection.</p> <p>2 MS. BROWN: Calls for speculation.</p> <p>3 THE WITNESS: I don't know their</p> <p>4 selection process, but they -- but they certainly</p> <p>5 invite -- invite people to attend.</p> <p>6 BY MS. PARFITT:</p> <p>7 Q Okay. Have you ever been invited to</p> <p>8 attend an IARC --</p> <p>9 A I have not.</p> <p>10 Q -- working group?</p> <p>11 A No.</p> <p>12 Q Okay. Did IARC invite you to attend</p> <p>13 their working group back in 2006 when they were</p> <p>14 deliberating on the issue of talcum -- talc</p> <p>15 products?</p> <p>16 MS. BROWN: Objection. Same question,</p> <p>17 asked and answered.</p> <p>18 THE WITNESS: She's right, but -- but</p> <p>19 no.</p> <p>20 BY MS. PARFITT:</p> <p>21 Q Okay. Did IARC ever invite you to</p> <p>22 attend and share your opinions when they had their</p> <p>23 asbestos meetings?</p> <p>24 MS. BROWN: Same objection.</p> <p>25 THE WITNESS: No.</p>

66 (Pages 258 to 261)

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 262</p> <p>1 BY MS. PARFITT:</p> <p>2 Q Do you know what the NTP is?</p> <p>3 A It's like the National Toxicological</p> <p>4 Program.</p> <p>5 Q Okay. Has the National Toxicological</p> <p>6 Program ever asked you to do research for them on</p> <p>7 talcum powder products?</p> <p>8 A No.</p> <p>9 Q Has the National Toxicology Program ever</p> <p>10 asked that you do research with them on asbestos?</p> <p>11 A No.</p> <p>12 Q Have you ever submitted any research to</p> <p>13 the NTP on anything?</p> <p>14 A No.</p> <p>15 Q Have you ever submitted any research to</p> <p>16 IARC on anything?</p> <p>17 A No.</p> <p>18 Q What is a risk factor?</p> <p>19 MS. BROWN: Objection to the form.</p> <p>20 THE WITNESS: Are we talking about like</p> <p>21 an epidemiologic definition?</p> <p>22 BY MS. PARFITT:</p> <p>23 Q Just generally, what's a risk factor?</p> <p>24 MS. BROWN: Objection.</p> <p>25 THE WITNESS: Well, I don't -- you said</p>	<p style="text-align: right;">Page 264</p> <p>1 Q For instance, if -- is talcum powder a</p> <p>2 modifiable behavior -- the use of talcum powder a</p> <p>3 modifiable behavior?</p> <p>4 MS. BROWN: Objection. Misstates his</p> <p>5 prior testimony.</p> <p>6 THE WITNESS: So it -- it should be,</p> <p>7 yeah.</p> <p>8 BY MS. PARFITT:</p> <p>9 Q Okay. Now, Dr. Diette, your paper or</p> <p>10 your expert report was signed and executed by you</p> <p>11 on February 25th, 2019.</p> <p>12 A Correct.</p> <p>13 Q Okay. When did you actually finish the</p> <p>14 paper, the report?</p> <p>15 A Oh, I think about then. I mean --</p> <p>16 Q About then?</p> <p>17 A I think around then. I mean it's -- I</p> <p>18 don't know whether it was the day before or the --</p> <p>19 or that actual day, but -- but right around then.</p> <p>20 Q Okay. Are you aware that -- I guess it</p> <p>21 was just a couple of months earlier that Health</p> <p>22 Canada issued and published a critical review and</p> <p>23 assessment of the science, which actually included</p> <p>24 a comprehensive review of the epidemiological</p> <p>25 literature? Did you know that?</p>
<p style="text-align: right;">Page 263</p> <p>1 generally. It could mean a million things to</p> <p>2 different people.</p> <p>3 BY MS. PARFITT:</p> <p>4 Q What's it mean to you?</p> <p>5 A It depends upon the context. That's why</p> <p>6 I'm asking from like an epidemiologic standpoint</p> <p>7 as opposed to some other context.</p> <p>8 Q Well, let's take mesothelioma. What are</p> <p>9 the risk factors for mesothelioma?</p> <p>10 A Well, if we're talking about, you know,</p> <p>11 asbestos, for example, as one risk factor, then</p> <p>12 you could use it that way, that -- that an</p> <p>13 exposure elevates the risk of developing a</p> <p>14 disease.</p> <p>15 Q Okay. Let's take talcum powder. Is</p> <p>16 talcum powder a risk factor for ovarian cancer?</p> <p>17 A I don't believe so.</p> <p>18 Q Are there risk factors that are</p> <p>19 modifiable?</p> <p>20 MS. BROWN: Objection to the form.</p> <p>21 THE WITNESS: For what?</p> <p>22 BY MS. PARFITT:</p> <p>23 Q For a disease.</p> <p>24 MS. BROWN: Same objection.</p> <p>25 BY MS. PARFITT:</p>	<p style="text-align: right;">Page 265</p> <p>1 MR. LOCKE: Objection.</p> <p>2 MS. BROWN: Objection. That misstates</p> <p>3 the draft assessment.</p> <p>4 THE WITNESS: I'm familiar with it.</p> <p>5 BY MS. PARFITT:</p> <p>6 Q Okay. Have you read it?</p> <p>7 A I have.</p> <p>8 Q Have you read it in its entirety?</p> <p>9 A I don't remember if there's like</p> <p>10 appendices or something, but I read all the -- you</p> <p>11 know, the mean part of the text.</p> <p>12 Q Okay. There is also meta-analysis that</p> <p>13 was performed about that same time.</p> <p>14 A Yes. Yeah.</p> <p>15 Q Have you read that?</p> <p>16 A I have.</p> <p>17 Q Okay. Did Health Canada do what we</p> <p>18 would refer to in your world of epidemiology a</p> <p>19 causality assessment?</p> <p>20 MS. BROWN: Objection to the form of the</p> <p>21 question.</p> <p>22 THE WITNESS: I don't know if that's</p> <p>23 what they did.</p> <p>24 BY MS. PARFITT:</p> <p>25 Q What did they do?</p>

67 (Pages 262 to 265)

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 266</p> <p>1 MS. BROWN: Objection.</p> <p>2 THE WITNESS: It looks to me as if they</p> <p>3 create -- well, so I don't know. So they -- they</p> <p>4 have their own process. I don't know anything</p> <p>5 about Health Canada, so I don't know what they</p> <p>6 typically do. You know, I've never -- it's unlike</p> <p>7 some other entities where I would kind of</p> <p>8 understand their process because I've read their</p> <p>9 things before.</p> <p>10 I don't -- I don't know anybody</p> <p>11 personally that looks to Health Canada for</p> <p>12 information, so I've never had a conversation with</p> <p>13 anybody about, you know, what their methods are,</p> <p>14 how they go about their business.</p> <p>15 But it looks as if what they were trying</p> <p>16 to do was to try to line up whether there was</p> <p>17 information about where talcum powder is found in</p> <p>18 Canada, so meaning like, you know, how many</p> <p>19 different kinds of products. It looked like they</p> <p>20 were trying to assess some things about dermal</p> <p>21 absorption or not, whether it's ingested or not,</p> <p>22 whether it's inhaled, whether perineal application</p> <p>23 matters or not.</p> <p>24 It seems that they commissioned yet</p> <p>25 another meta-analysis of some sort by Dr. Taher,</p>	<p style="text-align: right;">Page 268</p> <p>1 fair?</p> <p>2 MS. BROWN: Objection to the form.</p> <p>3 THE WITNESS: That looks to be part of</p> <p>4 what they've included in here.</p> <p>5 BY MS. PARFITT:</p> <p>6 Q And you yourself, for purposes of your</p> <p>7 report, looked at case-control studies, cohort</p> <p>8 studies, and meta-analyses, correct?</p> <p>9 A I did.</p> <p>10 Q Okay. Did Health Canada perform a</p> <p>11 Bradford Hill assessment of the evidence?</p> <p>12 MS. BROWN: Objection to the form.</p> <p>13 THE WITNESS: They have a section here.</p> <p>14 I mean, there's something here that -- that</p> <p>15 resembles a Bradford Hill analysis.</p> <p>16 BY MS. PARFITT:</p> <p>17 Q Okay. Let me direct your --</p> <p>18 MS. BROWN: Take as long as you need,</p> <p>19 Doctor, to finish your answer.</p> <p>20 THE WITNESS: Well, I just -- like I</p> <p>21 don't know -- I don't know how much leeway there</p> <p>22 is in the world for people to say that they did a</p> <p>23 Bradford Hill analysis just by listing out certain</p> <p>24 keywords, right? I mean it's sort of like a word</p> <p>25 salad exercise to me for some of these cases, and</p>
<p style="text-align: right;">Page 267</p> <p>1 and -- and then created the document that I guess</p> <p>2 that they put out there for -- for public comment</p> <p>3 of some sort.</p> <p>4 BY MS. PARFITT:</p> <p>5 Q Okay. All right. Let's have marked the</p> <p>6 Health Canada report, the draft assessment. And</p> <p>7 we'll have that marked as Exhibit No. 14.</p> <p>8 (Diette Exhibit No. 14 was marked</p> <p>9 for identification.)</p> <p>10 (Counsel conferring.)</p> <p>11 BY MS. PARFITT:</p> <p>12 Q Do you have that in front of you?</p> <p>13 A I do.</p> <p>14 Q Okay. All right. Did the -- did Health</p> <p>15 Canada look at all three types of study designs?</p> <p>16 And by that, I mean case control, cohort, and</p> <p>17 meta-analyses.</p> <p>18 MS. BROWN: Objection to what you mean</p> <p>19 by "look at." Objection to the form.</p> <p>20 THE WITNESS: They've listed -- they've</p> <p>21 listed some of each.</p> <p>22 BY MS. PARFITT:</p> <p>23 Q All right. So they consider for</p> <p>24 purposes of their analysis cohort studies,</p> <p>25 case-control studies and meta-analyses. Is that</p>	<p style="text-align: right;">Page 269</p> <p>1 so --</p> <p>2 BY MS. PARFITT:</p> <p>3 Q I'm sorry. A word what?</p> <p>4 A Word salad.</p> <p>5 Q Word salad.</p> <p>6 A Yeah. Not a technical term, but it's</p> <p>7 kind of a mess, right. So they've got -- like on</p> <p>8 page 19, they've got strength, and strength is a</p> <p>9 Bradford Hill criterion. They don't say whether</p> <p>10 the risk is, you know, weak or strong. They just</p> <p>11 have a list of 30 epidemiologic studies, and they</p> <p>12 say a couple things about some of them being</p> <p>13 statistically significant and -- and so forth.</p> <p>14 Q Okay.</p> <p>15 A And so that -- that isn't really a</p> <p>16 Bradford Hill type analysis about what the --</p> <p>17 whether the strength is high or low.</p> <p>18 And similarly, I would just say like,</p> <p>19 you know, for temporality, you know, what they've</p> <p>20 said here is crazy, right. So it's like --</p> <p>21 Q I'm sorry. What they've said here is</p> <p>22 what?</p> <p>23 A Crazy.</p> <p>24 Q Crazy.</p> <p>25 A Crazy.</p>

68 (Pages 266 to 269)

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 270</p> <p>1 Q So let me just ask --</p> <p>2 MS. BROWN: Wait now, he is not done.</p> <p>3 You can follow up when he is done with --</p> <p>4 MS. PARFITT: Fair enough.</p> <p>5 MS. BROWN: Go ahead, Doctor.</p> <p>6 BY MS. PARFITT:</p> <p>7 Q Okay. Crazy.</p> <p>8 A Okay. Oh, well, they said like in all</p> <p>9 case-control studies reporting positive outcomes,</p> <p>10 the participants recalled the exposure to talc</p> <p>11 preceded the reported outcome. I mean that is so</p> <p>12 far afield from any realistic epidemiologic</p> <p>13 principle that to say that that somehow informs a</p> <p>14 Bradford Hill analysis -- I don't know, maybe</p> <p>15 "crazy" is the wrong word. Maybe absurd, maybe</p> <p>16 ridiculous. But every person in the world that</p> <p>17 has a particular event or outcome, everything</p> <p>18 about them preceded them. That isn't the same as</p> <p>19 temporality. Temporality in the epidemiologic</p> <p>20 world is demonstrating that time flowed from the</p> <p>21 time of the exposure.</p> <p>22 So, that's why I say like -- you know, I</p> <p>23 read the words here, I see consistency,</p> <p>24 specificity, and so forth, but I don't think their</p> <p>25 application to this is actually a legitimate</p>	<p style="text-align: right;">Page 272</p> <p>1 Did I read that correctly?</p> <p>2 MS. BROWN: You didn't, and actually you</p> <p>3 said "consistently" and the word is "consistent."</p> <p>4 MS. PARFITT: Thank you.</p> <p>5 BY MS. PARFITT:</p> <p>6 Q Did I read that correctly with that</p> <p>7 correction?</p> <p>8 A Yes.</p> <p>9 Q Okay. Do you see where the authors</p> <p>10 state that, "Further available data are indicative</p> <p>11 of a causal effect"? Do you see that?</p> <p>12 A I do.</p> <p>13 Q Do you agree with Health Canada that</p> <p>14 there was a causal effect drawn from the genital</p> <p>15 use of talcum powder products and ovarian cancer?</p> <p>16 MS. BROWN: Objection to the form,</p> <p>17 misstates the draft assessment, lacks foundation.</p> <p>18 THE WITNESS: I don't think so, but for</p> <p>19 the reason that -- being that this is -- this is</p> <p>20 at some level -- maybe it's a summary, I don't</p> <p>21 know -- of what they have from above. But their</p> <p>22 input information into what they're concluding</p> <p>23 here is not good. Right.</p> <p>24 I mean look -- look up a couple of</p> <p>25 sentences under "Biologic plausibility," and they</p>
<p style="text-align: right;">Page 271</p> <p>1 Bradford Hill analysis.</p> <p>2 Q All right. So it's absurd, it's crazy,</p> <p>3 and your opinion is that they did not do a proper</p> <p>4 Bradford Hill analysis. Is that your opinion?</p> <p>5 A It is.</p> <p>6 MR. LOCKE: Objection.</p> <p>7 MS. BROWN: Objection to the form.</p> <p>8 BY MS. PARFITT:</p> <p>9 Q Okay. All right. Let me direct -- did</p> <p>10 they -- let me direct your attention to page 21.</p> <p>11 And we'll put that up on the ELMO.</p> <p>12 All right. Do you see that? Okay?</p> <p>13 A I'm on page 21.</p> <p>14 Q Page 21, and it's the last paragraph,</p> <p>15 and I'll read it.</p> <p>16 "The most recent meta-analysis detailed</p> <p>17 above, Taher, et al., 2018, and consistent with</p> <p>18 the Hill criteria, suggests a small but</p> <p>19 consistently statistically significant positive</p> <p>20 association between ovarian cancer and perineal</p> <p>21 exposure to talc. Further available data are</p> <p>22 indicative of a causal effect. A clear point of</p> <p>23 departure could not be derived from the available</p> <p>24 literature. Consequently, hazard characterization</p> <p>25 is qualitative in nature."</p>	<p style="text-align: right;">Page 273</p> <p>1 say: "The presence of talc in the ovaries has</p> <p>2 been documented," and cite Heller. And they say,</p> <p>3 "The evidence of retrograde transport supports the</p> <p>4 biologic plausibility."</p> <p>5 That Heller study doesn't -- doesn't</p> <p>6 support that, right. So they're -- they're</p> <p>7 stringing things together here that don't</p> <p>8 literally support I think a conclusive statement</p> <p>9 here.</p> <p>10 And also I would just say too, that when</p> <p>11 they say that -- that with the last part of that</p> <p>12 part you read where it says that "The hazard</p> <p>13 characterization is qualitative in nature," well,</p> <p>14 "qualitative" doesn't tell you something about</p> <p>15 whether it's a strong association. I mean they --</p> <p>16 they've resisted using that -- that word here.</p> <p>17 BY MS. PARFITT:</p> <p>18 Q Okay. So my question for you,</p> <p>19 Dr. Diette, is do you disagree with the draft</p> <p>20 Health Canada assessment which found that there</p> <p>21 was a causal relationship between the use of</p> <p>22 genital talcum powder products and ovarian cancer?</p> <p>23 MS. BROWN: Objection. That's not what</p> <p>24 the draft assessment --</p> <p>25 MS. PARFITT: Counsel, objection, form.</p>

Gregory B. Diette, M.D.

Page 274	Page 276
<p>1 MS. BROWN: You're -- it misstates the 2 document intentionally attempting to mislead the 3 witness. 4 MS. PARFITT: Objection. 5 THE WITNESS: So I -- first of all, 6 so -- 7 BY MS. PARFITT: 8 Q And, Doctor, let me just say something. 9 You can explain, but -- I have a question, and 10 then you can explain it if you wish. 11 And my question is, do you disagree with 12 the draft Health Canada assessment which found or 13 concluded that there was a causal relationship 14 between the use of genital talcum powder product 15 and ovarian cancer? 16 MR. LOCKE: Objection. 17 MS. BROWN: Objection to the form. 18 You can answer it truthfully and 19 accurately. 20 THE WITNESS: I can't answer it. 21 BY MS. PARFITT: 22 Q You can't -- wait one second. 23 A I cannot answer it. 24 Q You can't answer the question as to 25 whether or not you agree that they concluded that</p>	<p>1 talcum powder products used in the genital area 2 and ovarian cancer? That's the question. 3 MS. BROWN: Objection to the form of the 4 question, misstates the document -- 5 BY MS. PARFITT: 6 Q You may answer. 7 A Is there a specific sentence in there 8 that says that? 9 Q It's the question that I've asked you. 10 A Oh, so I can't answer it. I can answer 11 the -- 12 Q Is there a specific question -- 13 MS. BROWN: Wait, wait, let him finish. 14 BY MS. PARFITT: 15 Q -- 20, 21, 28, and Roman numeral iii? 16 MS. BROWN: What? 17 THE WITNESS: If there's a specific 18 sentence that says that, and you want me to agree 19 or disagree, I can agree or disagree with that 20 sentence. 21 What I can't agree with is an entire 22 document because I think it's not fair. I'm not 23 talking about just this one. I think, you know, 24 lawyers like to do this, right. They like to say, 25 Do you agree with a such-and-such paper. Well,</p>
Page 275	Page 277
<p>1 there was a causal relationship between talcum 2 powder products and ovarian cancer? 3 A So that -- 4 MS. BROWN: Objection to the form, 5 misstates the document. 6 Go ahead, Doctor. 7 THE WITNESS: Yeah, your question has 8 morphed, right. And so I'm still stuck on the way 9 it came out when you first said it. 10 BY MS. PARFITT: 11 Q Then let's go -- we'll go with the one 12 the -- 13 MS. BROWN: Wait, let him finish. 14 MS. PARFITT: No. Excuse me. 15 MS. BROWN: Counsel, you've been doing 16 that all day. You cannot cut this witness off. 17 He needs to finish. 18 MS. PARFITT: I'm not -- he asked for 19 what question I wanted to ask, so let me ask it 20 again. 21 BY MS. PARFITT: 22 Q Do you have -- is it -- do you -- strike 23 that. 24 Do you agree or disagree with Health 25 Canada and their assessment of causality between</p>	<p>1 it's nonsense. You don't agree with the paper. 2 You agree with the finding or you agree with the 3 conclusion, but not with the entire thing. 4 So here what I'm saying is, there's an 5 entire document here. There's some good stuff and 6 some bad stuff, and I can point out some of -- 7 some of each. 8 But the point here is if there's a 9 specific statement that they made that says -- 10 about causation, I would just like to see that 11 particular statement and tell you whether I can 12 agree with it or not. 13 BY MS. PARFITT: 14 Q Well, look at page 28 -- or excuse me, 15 21, the page we were on. 16 Do you have that in front of you? 17 A I do. 18 Q Okay. "Available data are 19 indicative" -- 20 MS. BROWN: Counsel, where are you? 21 MS. PARFITT: It's the paragraph just 22 above "Exposure Assessment." It says the recent 23 -- we just read it. 24 BY MS. PARFITT: 25 Q "The most recent meta-analysis detailed</p>

70 (Pages 274 to 277)

Gregory B. Diette, M.D.

Page 278	Page 280
<p>1 above, Taher, and consistent with the Hill</p> <p>2 criteria, suggests a small but consistent</p> <p>3 statistically significant positive association</p> <p>4 between ovarian cancer and perineal exposure to</p> <p>5 talc. Further available data are indicative of a</p> <p>6 causal effect."</p> <p>7 MS. BROWN: What's the question?</p> <p>8 BY MS. PARFITT:</p> <p>9 Q Do you agree with the conclusions of</p> <p>10 Health Canada?</p> <p>11 MS. BROWN: Objection to the form. This</p> <p>12 is not the conclusion section.</p> <p>13 THE WITNESS: So, first of all, the --</p> <p>14 the first sentence that you read there talks about</p> <p>15 a significant positive association, which isn't</p> <p>16 the same as cause. Right. And then they say,</p> <p>17 "Further available data are indicative of..."</p> <p>18 I -- I think if you're trying to say</p> <p>19 that something causes something, you come out and</p> <p>20 you say it. You don't say, "Further data are</p> <p>21 indicative of it." So I -- I don't think this</p> <p>22 statement says talcum powder causes ovarian</p> <p>23 cancer.</p> <p>24 BY MS. PARFITT:</p> <p>25 Q Okay. So your quarrel with Health</p>	<p>1 A That sentence is there.</p> <p>2 Q All right. Okay.</p> <p>3 MS. BROWN: Counsel, if you're moving to</p> <p>4 another area, would --</p> <p>5 MS. PARFITT: I am.</p> <p>6 MS. BROWN: Would this be a good time</p> <p>7 for a break?</p> <p>8 MS. PARFITT: Yeah. I'm going to move</p> <p>9 on and change gears.</p> <p>10 THE VIDEOGRAPHER: The time is 1:52</p> <p>11 p m., and we are off the record.</p> <p>12 (Recess.)</p> <p>13 THE VIDEOGRAPHER: The time is</p> <p>14 2:04 p m., and we're back on the record.</p> <p>15 BY MS. PARFITT:</p> <p>16 Q Dr. Diette, you mentioned before the</p> <p>17 break the Heller article, and so I don't misquote</p> <p>18 you, what was your position with regard to Heller</p> <p>19 and what it stood for?</p> <p>20 A I think if we're talking about the --</p> <p>21 the right one, it's the one where the ovaries were</p> <p>22 removed from, I think, 24 women, and that 12 -- 12</p> <p>23 had said that they were talcum powder users and 12</p> <p>24 not, but they found a -- they found a similar</p> <p>25 amount of talc in ovaries regardless of whether</p>
Page 279	Page 281
<p>1 Canada is the fact that they didn't say it, Talcum</p> <p>2 powder products used in the genital area cause</p> <p>3 ovarian cancer.</p> <p>4 A Well --</p> <p>5 Q You quarrel with their language. Is</p> <p>6 that what you're saying?</p> <p>7 A Well, I quarrel --</p> <p>8 MS. BROWN: Objection. Misstates his</p> <p>9 testimony.</p> <p>10 THE WITNESS: I quarrel a little with</p> <p>11 you, I think -- I'm sorry.</p> <p>12 THE REPORTER: I'm sorry, your --</p> <p>13 MS. BROWN: I just want to object to the</p> <p>14 question as misstating your testimony.</p> <p>15 THE WITNESS: Because I think your</p> <p>16 initial question before you read it literally was</p> <p>17 about whether or not they said that it causes it,</p> <p>18 and I don't think that it said that.</p> <p>19 And -- and I think otherwise that there</p> <p>20 are some flaws in the -- in the information that</p> <p>21 they've used up above to reach this -- I guess</p> <p>22 it's a conclusion. I don't know if it is or not.</p> <p>23 BY MS. PARFITT:</p> <p>24 Q Okay. Does it say, "Further available</p> <p>25 data are indicative of a causal effect"?</p>	<p>1 they were users or not.</p> <p>2 Q Okay. Is -- is it your opinion that</p> <p>3 talc cannot migrate to the ovaries?</p> <p>4 A I don't know that it can. I -- if it's</p> <p>5 found there, I'm not sure how it got there.</p> <p>6 Q Is it your opinion that asbestos can</p> <p>7 migrate to the ovaries?</p> <p>8 MS. BROWN: Objection to the form.</p> <p>9 THE WITNESS: I've seen -- I don't think</p> <p>10 I've seen anything that shows for sure that it</p> <p>11 can.</p> <p>12 BY MS. PARFITT:</p> <p>13 Q Okay. If asbestos was found in the</p> <p>14 ovaries, how would it get there?</p> <p>15 MS. BROWN: Objection to the form.</p> <p>16 THE WITNESS: So I don't know. I mean,</p> <p>17 it's -- I don't know of a worked-out mechanism</p> <p>18 that shows how it got there.</p> <p>19 (Diette Exhibit No. 15 was marked</p> <p>20 for identification.)</p> <p>21 BY MS. PARFITT:</p> <p>22 Q Let me show you what's been marked as</p> <p>23 Heller Exhibit No. 15. And it is a 1996 article</p> <p>24 entitled "Asbestos Exposure and Ovarian Fiber</p> <p>25 Burden."</p>

71 (Pages 278 to 281)

Gregory B. Diette, M.D.

Page 282	Page 284
<p>1 (Counsel conferring.)</p> <p>2 BY MS. PARFITT:</p> <p>3 Q Do you have that in front of you?</p> <p>4 A I do.</p> <p>5 Q All right. Now, this was a different</p> <p>6 Heller article than the one you were referring to?</p> <p>7 A Thank you, yes.</p> <p>8 Q Okay. All right. Now, let me direct</p> <p>9 your attention to the Abstract section, the last</p> <p>10 paragraph.</p> <p>11 Okay. And it states: "This study</p> <p>12 demonstrates that asbestos can reach the ovary.</p> <p>13 Although the number of subjects is small, asbestos</p> <p>14 appears to be present in ovarian tissue more</p> <p>15 frequently and in higher amounts in women with a</p> <p>16 documentable exposure history."</p> <p>17 Did I read that correctly?</p> <p>18 A Yes.</p> <p>19 Q All right. Do you agree with that</p> <p>20 statement?</p> <p>21 MS. BROWN: Objection to the form.</p> <p>22 THE WITNESS: Give me one sec, because</p> <p>23 I -- it's been a while since I looked at this.</p> <p>24 MS. BROWN: Take your time, Doctor.</p> <p>25 THE WITNESS: (Peruses document.) Yeah,</p>	<p>1 A And it's about the middle of the</p> <p>2 paragraph, and it says it is -- it says -- right</p> <p>3 above it, it says: "None of the exposed subjects</p> <p>4 in the study was directly occupationally exposed</p> <p>5 but all were passively exposed to household</p> <p>6 contact. It is unclear why so many of the women</p> <p>7 giving no exposure history did have detectable</p> <p>8 asbestos in their ovaries, although it is known</p> <p>9 that there is a background level of asbestos in</p> <p>10 the lung tissue of non-exposed individuals."</p> <p>11 So I -- I don't know. I just don't --</p> <p>12 that this -- this cements the idea that -- that we</p> <p>13 know something about how asbestos, you know, can</p> <p>14 get to the ovaries.</p> <p>15 Q All right. Let me direct your attention</p> <p>16 to the bottom of 438, top of 439.</p> <p>17 At the bottom of 438, it says "There</p> <p>18 is," and then it goes on to the top of 439:</p> <p>19 "There is evidence of transport of particulate</p> <p>20 matter into the female perineum by the</p> <p>21 transvaginal route."</p> <p>22 A I apologize, I -- I'm not with you, and</p> <p>23 I just --</p> <p>24 Q Oh, sure.</p> <p>25 A I'm just trying to --</p>
Page 283	Page 285
<p>1 again, like -- so not entirely.</p> <p>2 BY MS. PARFITT:</p> <p>3 Q What part -- what part --</p> <p>4 MS. BROWN: Let him finish.</p> <p>5 BY MS. PARFITT:</p> <p>6 Q What part do you agree with?</p> <p>7 A Well, the -- I think that it's -- it's</p> <p>8 not -- well, so the study demonstrates that</p> <p>9 asbestos can reach the ovary. I guess if it's</p> <p>10 definitely there, then -- and it got there somehow</p> <p>11 and it wasn't through contamination, you know, of</p> <p>12 the procedure that -- that led to it, you could --</p> <p>13 you know, you could infer that there's some way</p> <p>14 that it got there.</p> <p>15 I think it doesn't tell us anything</p> <p>16 about how to make sense of that. And what I was</p> <p>17 looking for that I remember is that they said that</p> <p>18 it's unclear why so many women giving no exposure</p> <p>19 history did have detectable asbestos in their</p> <p>20 ovaries.</p> <p>21 Q Where do you see that?</p> <p>22 A I'm sorry. I'm on 439.</p> <p>23 Q Thank you.</p> <p>24 A And in the Conclusion paragraph.</p> <p>25 Q Mm-hmm. Yes.</p>	<p>1 Q It's right here, upper corner, 439.</p> <p>2 A Got you.</p> <p>3 Q Okay?</p> <p>4 A Yep.</p> <p>5 Q All right, again. "There is evidence of</p> <p>6 transport of particulate matter into the female</p> <p>7 perineum by the transvaginal route in both human</p> <p>8 and animal studies." It cites Egli and Newton,</p> <p>9 1961. It cites Henderson, 1986; Venter -- and I'm</p> <p>10 sure I'll destroy this name -- Iturralde, 1979;</p> <p>11 Whittemore, 1988. "Suggested that vaginal</p> <p>12 exposure to particulate matter such as asbestos</p> <p>13 and talc was a potential risk factor for</p> <p>14 intraperitoneal ovarian exposure. Her conclusion</p> <p>15 was based on finding that in talc exposed women, a</p> <p>16 previous history of hysterectomy or tubal</p> <p>17 ligation, which blocks perineum access, was</p> <p>18 protective against ovarian cancer."</p> <p>19 It goes on to say: "Talc has been</p> <p>20 implicated as a possible etiological agent in</p> <p>21 ovarian cancer," citing Harlow '89 and '92, "and</p> <p>22 is related to the asbestos problem in several</p> <p>23 ways. Aside from the chemical similarities</p> <p>24 between the two, many cosmetic talcs contained</p> <p>25 significant amounts of asbestos, particularly</p>

72 (Pages 282 to 285)

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 286</p> <p>1 prior to '70 -- 1976, Cramer, 1982. The</p> <p>2 significance of this detection of talc in the</p> <p>3 majority of exposed women and in all women giving</p> <p>4 no exposure history is unclear and further studies</p> <p>5 are underway to further elucidate this question."</p> <p>6 Did I read that correctly?</p> <p>7 A Yes.</p> <p>8 Q Question: Are there chemical</p> <p>9 similarities between cosmetic talcs and asbestos?</p> <p>10 MS. BROWN: Objection to the form.</p> <p>11 THE WITNESS: So some of the same --</p> <p>12 some of the same features chemically are present</p> <p>13 in both.</p> <p>14 BY MS. PARFITT:</p> <p>15 Q All right. Set that aside for a minute.</p> <p>16 We may come back to that.</p> <p>17 Dr. Diette, for purposes of your</p> <p>18 opinions in this case, you have stated that the</p> <p>19 cohort studies lack statistical significance, and</p> <p>20 only a subset of the case-control studies are</p> <p>21 statistically significant. Therefore, there is a</p> <p>22 disparity and inconsistency between cohorts and</p> <p>23 case control.</p> <p>24 Have I summed it up pretty well?</p> <p>25 A That -- that's one of the -- one of the</p>	<p style="text-align: right;">Page 288</p> <p>1 If you know.</p> <p>2 THE WITNESS: Can I assume or --</p> <p>3 MS. BROWN: No, if you don't know, don't</p> <p>4 answer. Then you have no basis to answer the</p> <p>5 question.</p> <p>6 BY MS. PARFITT:</p> <p>7 Q My question is, do you know what Ken</p> <p>8 Rothman's area of expertise is?</p> <p>9 MS. BROWN: Objection.</p> <p>10 THE WITNESS: Well, he's -- he's made a</p> <p>11 career out of -- out of case-control studies and</p> <p>12 articulating, you know, features of the design and</p> <p>13 so forth.</p> <p>14 BY MS. PARFITT:</p> <p>15 Q All right. Is he an epidemiologist?</p> <p>16 A Well, that's what I was trying to</p> <p>17 remember. Like, I would only be guessing. Like,</p> <p>18 I assume for him to be in that role, he would be,</p> <p>19 but there are people that come to epidemiology</p> <p>20 from other -- you know, other backgrounds, and so</p> <p>21 I just don't know his credentials.</p> <p>22 Q Okay. What about Sander Greenland, do</p> <p>23 you know who he is?</p> <p>24 A I know the name, but I don't know him.</p> <p>25 Q Okay. Have you ever -- do you know what</p>
<p style="text-align: right;">Page 287</p> <p>1 bits of evidence of inconsistency.</p> <p>2 Q Okay. Would you agree that to disregard</p> <p>3 study results based upon whether they are</p> <p>4 statistically significant or not statistically</p> <p>5 significant would be a mistake?</p> <p>6 MS. BROWN: Objection to the form.</p> <p>7 Counsel, is there something you're reading from</p> <p>8 that --</p> <p>9 MS. PARFITT: No. Actually, my notes,</p> <p>10 and he doesn't get those. Thank you.</p> <p>11 THE WITNESS: Okay. So "disregard" is</p> <p>12 pretty severe. Right. So I don't think that</p> <p>13 somebody should disregard any study, unless it's,</p> <p>14 you know, fraudulent or, you know, created out of</p> <p>15 nowhere. So I think that people should regard the</p> <p>16 findings and interpret them appropriately.</p> <p>17 So I think that would be an overly</p> <p>18 strong thing to do, which would be to disregard it</p> <p>19 simply because it's statistically insignificant.</p> <p>20 BY MS. PARFITT:</p> <p>21 Q Okay. Do you know who Ken Rothman is?</p> <p>22 A I -- I know of him. I don't know him</p> <p>23 personally.</p> <p>24 Q Okay. What does he do for a living?</p> <p>25 MS. BROWN: Objection to the form.</p>	<p style="text-align: right;">Page 289</p> <p>1 kind of scientist Sander Greenland is?</p> <p>2 MS. BROWN: Objection. Form.</p> <p>3 THE WITNESS: I do not.</p> <p>4 MS. BROWN: Foundation.</p> <p>5 BY MS. PARFITT:</p> <p>6 Q Okay. All right. Do you know Timothy</p> <p>7 Lash?</p> <p>8 MS. BROWN: Objection. Foundation.</p> <p>9 THE WITNESS: I don't know the name.</p> <p>10 BY MS. PARFITT:</p> <p>11 Q Okay. Do you know what kind of</p> <p>12 scientist Tim -- Timothy Lash is?</p> <p>13 MS. BROWN: Same objection.</p> <p>14 THE WITNESS: It would be hard to know</p> <p>15 that --</p> <p>16 BY MS. PARFITT:</p> <p>17 Q Okay.</p> <p>18 A -- without knowing him.</p> <p>19 Q Okay. Let me show you what we will have</p> <p>20 marked as Exhibit No. -- 61? 16.</p> <p>21 MR. TISI: We're not that high.</p> <p>22 (Diette Exhibit No. 16 was marked</p> <p>23 for identification.)</p> <p>24 BY MS. PARFITT:</p> <p>25 Q And I will -- and I will represent,</p>

73 (Pages 286 to 289)

Gregory B. Diette, M.D.

Page 290	Page 292
<p>1 Dr. Diette, that this is Chapter 2 out of the 2 Third Edition, Modern Epidemiology. 3 Do you see that? 4 A I do. 5 Q Okay. And if you look at the front of 6 it, it has three authors. 7 Do you see that? 8 A I do. 9 Q Okay. The first one is Ken Rothman. Do 10 you see that? 11 A Correct. 12 Q The second one is Sander Greenland. 13 A Correct. 14 Q And the third author is Tim Lash. Do 15 you see that? 16 A I do. 17 Q And they are -- the book that they have 18 authored is called Modern Epidemiology, Third 19 Edition. Do you see that? 20 A I do. 21 Q Okay. Let me -- let me direct your 22 attention to page 27. 23 MS. BROWN: Counsel, are you going to 24 lay a foundation for the use of this document? 25 MS. PARFITT: I can just ask a question.</p>	<p>1 MS. BROWN: I have a continuing 2 foundation. 3 MS. PARFITT: That's fine, Counsel. 4 MS. BROWN: -- objection to this 5 exhibit, for which no foundation has been laid. 6 BY MS. PARFITT: 7 Q All right. Again, I'm referring to the 8 category consistency which I represent that is in 9 Chapter 2 of the Rothman book, and we can just go 10 ahead and circle the paragraph that starts: "One 11 mistake in implementing the consistency criterion 12 is so common that it deserves special mention. It 13 is sometimes claimed that a literature or set of 14 results is inconsistent simply because some 15 results are statistically significant, and some 16 are not." 17 Did I read that correctly? 18 A You did. 19 Q "This sort of evaluation is completely 20 fallacious, even if one accepts the use of 21 significant testing methods." 22 Did I read that correctly? 23 A You did. 24 Q All right. Do you agree with that 25 statement?</p>
Page 291	Page 293
<p>1 I can do that. 2 BY MS. PARFITT: 3 Q Let me ask a question. 4 "To claim that literature, scientific 5 literature, or a set of results reported in 6 scientific literature is inconsistent simply 7 because some results are statistically 8 significant, and some are not, would be completely 9 fallacious, even if one accepts the use of 10 significant testing methods." 11 Do you agree with that statement? 12 MR. LOCKE: Objection. 13 MS. BROWN: Objection. Form, 14 foundation. 15 THE WITNESS: Is that a hybrid of a 16 couple of things? Because I thought I was reading 17 with you, and then I might have left off. 18 BY MS. PARFITT: 19 Q Well, why don't we do this. We'll put 20 it back on the ELMO, and I'll represent that it is 21 a -- 22 A Yeah, I don't doubt you. I just -- 23 Q Sure, no worries. That's fine. 24 A It goes on to a different sentence. 25 Q That's fine.</p>	<p>1 MR. LOCKE: Objection. 2 THE WITNESS: So wait a minute, I just 3 want to -- so there's a couple of statements 4 there. I think the part that makes it agreeable 5 is to say that -- that if it's claimed that 6 results are -- and I'm paraphrasing -- 7 BY MS. PARFITT: 8 Q Sure. 9 A -- but that the results are inconsistent 10 simply, and the word "simply" to me is really 11 important here because it suggests that somebody 12 would be not looking at the entire universe of 13 evidence that they have available. 14 So I think if you just took a quick look 15 at studies and said some were significant and some 16 weren't and left it at that, you know, it's a 17 pretty strong statement, but I think -- I think 18 that would be a mistake to only do that. 19 Q All right. Now, you're not a 20 statistician, correct? 21 A I'm not a statistician. 22 Q Okay. And you're not a biostatistician. 23 A I'm not a biostatistician. 24 Q Okay. Do you know who Daniel Ford is? 25 A I do.</p>

Gregory B. Diette, M.D.

Page 294	Page 296
<p>1 Q Okay. Who is Daniel Ford?</p> <p>2 A If it's the one that --</p> <p>3 Q Daniel E. Ford.</p> <p>4 A I don't know his middle name, but</p> <p>5 there's a Dan Ford at our -- at our place.</p> <p>6 Q Okay. Is the Dan Ford you know vice</p> <p>7 dean for clinical investigation, Johns Hopkins</p> <p>8 School of Medicine?</p> <p>9 A Yes.</p> <p>10 Q Okay. Is he a friend of yours?</p> <p>11 A We're friendly. I mean, we don't hang</p> <p>12 out, though.</p> <p>13 Q Now, he is with the Institute for</p> <p>14 Clinical and Translational Research; is that</p> <p>15 correct?</p> <p>16 A He has been. I'm just trying to think</p> <p>17 if that still exists. Because I know there was a</p> <p>18 funding issue, so -- but he -- he certainly was in</p> <p>19 that role, and he may still be.</p> <p>20 Q He may what?</p> <p>21 A He may still be. I just -- I just -- I</p> <p>22 thought I had heard that the ICTRs were going to</p> <p>23 be not funded anymore.</p> <p>24 Q Okay.</p> <p>25 A Maybe it's true, maybe not; but I'm just</p>	<p>1 Q Do you know about that?</p> <p>2 A I'm aware of that.</p> <p>3 Q Okay. Now, are you -- did you read</p> <p>4 Dr. Bowman's deposition?</p> <p>5 A I did.</p> <p>6 Q Okay. Did you see that in Dr. Bowman's</p> <p>7 deposition?</p> <p>8 A I saw -- I'm just trying to remember. I</p> <p>9 saw the Nature article, I think that is more</p> <p>10 recently published than -- you said 2016?</p> <p>11 Q Originally, yes.</p> <p>12 A Yeah, but I can't remember if 2016 was</p> <p>13 in her deposition, but for sure the more recent</p> <p>14 one.</p> <p>15 Q The one in 2019?</p> <p>16 A Exactly right, yeah.</p> <p>17 Q All right. All right. Let me show you</p> <p>18 then what's been marked as -- or will be marked as</p> <p>19 17. And it is the March 2019 --</p> <p>20 (Counsel conferring.)</p> <p>21 BY MS. PARFITT:</p> <p>22 Q Okay. Let me show you what we will have</p> <p>23 marked as 17, a study that appeared in The</p> <p>24 American Statistician in 2019. It's Volume 73,</p> <p>25 and it's called "Moving to a World Beyond P <</p>
Page 295	Page 297
<p>1 saying for sure he was part of that.</p> <p>2 Q Mm-hmm. Okay. Sure. Okay.</p> <p>3 All right. Are you a member -- and I'm</p> <p>4 assuming you're not because you're not a</p> <p>5 statistician, but I should assume nothing.</p> <p>6 Are you a member of the American</p> <p>7 Statistical Association?</p> <p>8 A I am not.</p> <p>9 Q Okay. Do you know who they are?</p> <p>10 A Not -- not really. I mean, it -- it</p> <p>11 sounds like the name gives them away, but I</p> <p>12 don't -- I don't know, you know, who they are as</p> <p>13 an entity otherwise.</p> <p>14 Q That's fair. Okay.</p> <p>15 Are you aware that due to a widespread</p> <p>16 misuse by scientists and researchers regarding</p> <p>17 statistical significance and p-values, that the</p> <p>18 American Statistical Association issued a</p> <p>19 statement back in 2016 warning the scientific</p> <p>20 community of this misuse and urging them to cease</p> <p>21 and desist with the p-value?</p> <p>22 MR. LOCKE: Objection.</p> <p>23 MS. BROWN: Objection to the form, lacks</p> <p>24 foundation, misrepresents the facts.</p> <p>25 BY MS. PARFITT:</p>	<p>1 0.05."</p> <p>2 Do you see that?</p> <p>3 A Actually, I was just sort of flipping</p> <p>4 through to see what I'm looking at. Oh, so the</p> <p>5 title, yes.</p> <p>6 Q Okay. Is this a document you were</p> <p>7 referring to?</p> <p>8 A No.</p> <p>9 Q No?</p> <p>10 A I was referring to the one in Nature</p> <p>11 that I think reports about this.</p> <p>12 Q Yes. Okay. Let's go ahead and get that</p> <p>13 marked, and we'll talk about all three.</p> <p>14 (Diette Exhibit No. 17 was marked</p> <p>15 for identification.)</p> <p>16 MS. PARFITT: Let's have marked as</p> <p>17 Exhibit No. 18.</p> <p>18 (Diette Exhibit No. 18 was marked</p> <p>19 for identification.)</p> <p>20 BY MS. PARFITT:</p> <p>21 Q And I will represent that 18 is a Sander</p> <p>22 Greenland article that appeared in Nature on</p> <p>23 March 2019.</p> <p>24 Okay. Is that the article you were</p> <p>25 referring to?</p>

75 (Pages 294 to 297)

Gregory B. Diette, M.D.

Page 298	Page 300
<p>1 A Yes.</p> <p>2 Q Okay. Have you had an opportunity to</p> <p>3 read Exhibit No. 18?</p> <p>4 A I have.</p> <p>5 Q Okay. Exhibit 17, which is the</p> <p>6 Wasserstein article, have you had an opportunity</p> <p>7 to read it prior to today?</p> <p>8 A This -- this one, no.</p> <p>9 Q Okay. All right. Let's first take a</p> <p>10 moment and discuss what's been marked as 18.</p> <p>11 Excuse me. No, 18. 18.</p> <p>12 Are you aware that due to the American</p> <p>13 Statistical Society's concern of the misuse of</p> <p>14 statistical significance and p-value, that they</p> <p>15 literally used their March 2019 research paper and</p> <p>16 devoted attention to this issue and attached</p> <p>17 almost 40 papers on statistical inference? Are</p> <p>18 you aware of that?</p> <p>19 MR. LOCKE: Objection.</p> <p>20 MS. BROWN: Objection to the form,</p> <p>21 misstates the facts. Are you referring to</p> <p>22 Exhibit 17?</p> <p>23 MS. PARFITT: No. 17. 17.</p> <p>24 MS. BROWN: Yes, 17.</p> <p>25 MS. PARFITT: No, I'm not referring to</p>	<p>1 MS. BROWN: -- before you ask him any</p> <p>2 questions about it.</p> <p>3 BY MS. PARFITT:</p> <p>4 Q I just have a couple of questions about</p> <p>5 it.</p> <p>6 MS. BROWN: Take as long as you need.</p> <p>7 THE WITNESS: (Peruses document.)</p> <p>8 BY MS. PARFITT:</p> <p>9 Q And I just have a couple of questions</p> <p>10 about it.</p> <p>11 A Sure.</p> <p>12 MS. BROWN: He's never seen it, so he</p> <p>13 needs --</p> <p>14 MS. PARFITT: That's fine.</p> <p>15 MS. BROWN: -- as long as he needs.</p> <p>16 MS. PARFITT: He can take -- yeah.</p> <p>17 THE WITNESS: Well, I won't be able to</p> <p>18 read it in --</p> <p>19 BY MS. PARFITT:</p> <p>20 Q Okay. Let me just --</p> <p>21 A -- in realtime today.</p> <p>22 Q -- ask you a couple of questions. I'm</p> <p>23 not expecting you to digest it.</p> <p>24 All right. The first paragraph, it</p> <p>25 says -- do you have it up there?</p>
Page 299	Page 301
<p>1 that at all. I'm just -- I'm asking a question.</p> <p>2 MS. BROWN: Objection. Lacks</p> <p>3 foundation, misstates the facts.</p> <p>4 THE WITNESS: I saw that there was a --</p> <p>5 a journal issue that had many articles. I</p> <p>6 didn't -- I don't know what the count was, but</p> <p>7 there -- it's probably the same thing we're</p> <p>8 talking about, but I'm not sure.</p> <p>9 BY MS. PARFITT:</p> <p>10 Q Okay. Did you have a chance to read</p> <p>11 those 40 or so articles?</p> <p>12 MS. BROWN: Objection to the form.</p> <p>13 THE WITNESS: I -- I wish I had that</p> <p>14 kind of time, but --</p> <p>15 BY MS. PARFITT:</p> <p>16 Q You and me both.</p> <p>17 A Yeah.</p> <p>18 Q Okay. All right. Let's stay a few</p> <p>19 minutes on 17, and we'll put it up on the ELMO.</p> <p>20 And it starts --</p> <p>21 MS. BROWN: Counsel, he's never seen 17</p> <p>22 before, so he's going to need a minute to</p> <p>23 familiarize himself with it --</p> <p>24 BY MS. PARFITT:</p> <p>25 Q Take a minute to familiarize yourself.</p>	<p>1 "Some of you exploring this special</p> <p>2 issue of The American Statistician might be</p> <p>3 wondering if it's a scolding from the pedantic</p> <p>4 statisticians lecturing you about what not to do</p> <p>5 with p-values, without offering any real ideas of</p> <p>6 what to do about the very hard problem separating</p> <p>7 signal from noise in data and making decisions</p> <p>8 under uncertainty. Fear not, in this issue,</p> <p>9 thanks to 43 innovative and thought-provoking</p> <p>10 papers from forward-looking statisticians, help is</p> <p>11 on the way."</p> <p>12 Do you see that?</p> <p>13 A I do.</p> <p>14 Q Okay. Did I read that correctly?</p> <p>15 A You did.</p> <p>16 Q And is that the 43 papers that you were</p> <p>17 speaking of that you didn't have time to read?</p> <p>18 MS. BROWN: Objection to the form, lacks</p> <p>19 foundation.</p> <p>20 THE WITNESS: I -- I think so. I mean,</p> <p>21 this sounds familiar. I think it's what I was</p> <p>22 looking at, but I'm not -- not a hundred percent</p> <p>23 sure.</p> <p>24 BY MS. PARFITT:</p> <p>25 Q Okay. If you'd look at right under</p>

76 (Pages 298 to 301)

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 302</p> <p>1 "Don't' is Not Enough." Do you see that?</p> <p>2 A Yes.</p> <p>3 Q All right. The first sentence says:</p> <p>4 "There's not much we can say here about the perils</p> <p>5 of p-values and significance testing that hasn't</p> <p>6 already -- that hasn't been said already for</p> <p>7 decades."</p> <p>8 Did I read that correctly?</p> <p>9 A Yes.</p> <p>10 Q And then it goes down to the first one:</p> <p>11 "Don't base your conclusions solely on whether an</p> <p>12 association or effect was found to be</p> <p>13 statistically significant. The p-value passed</p> <p>14 some arbitrary threshold such as $p < 0.05$."</p> <p>15 Did I read that correctly?</p> <p>16 A Yes.</p> <p>17 Q Do you agree with that statement?</p> <p>18 MR. LOCKE: Objection.</p> <p>19 THE WITNESS: So there's a lot to this,</p> <p>20 right. I mean because, I mean, the lead in to it,</p> <p>21 it says -- it says that there's not much to say</p> <p>22 here, you know --</p> <p>23 BY MS. PARFITT:</p> <p>24 Q That hasn't been said.</p> <p>25 A -- hasn't been said for decades.</p>	<p style="text-align: right;">Page 304</p> <p>1 statistical significance or lack thereof."</p> <p>2 Do you agree with that statement?</p> <p>3 MS. BROWN: Objection to the form.</p> <p>4 And, Doctor, if you need to read the</p> <p>5 whole article to answer these questions --</p> <p>6 MS. PARFITT: Counsel, don't coach the</p> <p>7 witness.</p> <p>8 MS. BROWN: -- you should do that.</p> <p>9 Yeah, but you are knowingly --</p> <p>10 BY MS. PARFITT:</p> <p>11 Q Go ahead, Doctor.</p> <p>12 MS. BROWN: -- putting a document in</p> <p>13 front of him that he's never seen, so we're not</p> <p>14 going to sit here --</p> <p>15 BY MS. PARFITT:</p> <p>16 Q I'm asking you a question, Dr. Diette --</p> <p>17 MS. BROWN: -- and play cherry-</p> <p>18 picking statements to get --</p> <p>19 BY MS. PARFITT:</p> <p>20 Q -- do you agree that one should not</p> <p>21 conclude anything about scientific or practical</p> <p>22 importance based on statistical significance or</p> <p>23 lack thereof? Do you agree with that?</p> <p>24 MR. LOCKE: Objection.</p> <p>25 MS. BROWN: Same objection.</p>
<p style="text-align: right;">Page 303</p> <p>1 MS. BROWN: Wait, wait, let him finish.</p> <p>2 THE WITNESS: And -- and that's --</p> <p>3 that's pretty -- well, I can't say it's true</p> <p>4 because I haven't read this, so I don't know</p> <p>5 what's in here, but the debate about p-values and</p> <p>6 statistical significance isn't brand new. I mean,</p> <p>7 I've been talking about it with colleagues for</p> <p>8 decades, and I'm sure there were people decades</p> <p>9 before me. So that -- that part rings true.</p> <p>10 And I think -- you know, I don't know</p> <p>11 when they're talking about conclusions. That's</p> <p>12 a -- that's a pretty broad topic, but I think the</p> <p>13 word "solely" is very helpful there, that we</p> <p>14 shouldn't be making decisions solely on whether</p> <p>15 something is statistically significant. And</p> <p>16 there's more to it than that.</p> <p>17 BY MS. PARFITT:</p> <p>18 Q Okay.</p> <p>19 A But that's a -- that's a super broad</p> <p>20 statement, and I don't know, you know, in every</p> <p>21 circumstance whether that would be agreeable or</p> <p>22 not.</p> <p>23 Q Okay. Look at the last bullet there.</p> <p>24 It states: "Don't conclude anything about</p> <p>25 scientific or practical importance based on</p>	<p style="text-align: right;">Page 305</p> <p>1 THE WITNESS: So, anyway, I think by</p> <p>2 saying "don't conclude anything," I think makes</p> <p>3 this not a very agreeable statement for me.</p> <p>4 BY MS. PARFITT:</p> <p>5 Q Okay. All right. Let's turn to what</p> <p>6 you did read, and that's Exhibit 18.</p> <p>7 Do you have that, Doctor?</p> <p>8 A I do.</p> <p>9 Q Okay. And this is an article that</p> <p>10 appeared in Nature back in March of 2019, correct?</p> <p>11 A That's right.</p> <p>12 Q Okay. And you did have a chance to read</p> <p>13 this; is that correct?</p> <p>14 A I did.</p> <p>15 Q Okay. And under the section "Pervasive</p> <p>16 Problem," do you see that?</p> <p>17 A Yes.</p> <p>18 Q Okay. It states: "Let's be clear about</p> <p>19 what must stop. We should never conclude there is</p> <p>20 no difference or no association just because the</p> <p>21 p-value is larger than the threshold, such as</p> <p>22 0.05, or equivalently because a confidence</p> <p>23 interval includes zero. Neither should we</p> <p>24 conclude that two studies conflict because one had</p> <p>25 a statistically significant result and the other</p>

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 306</p> <p>1 did not. These errors waste research efforts and 2 misinform policy decisions." 3 Did I read that correctly? 4 A You did. 5 Q Do you agree with that? 6 MS. BROWN: Objection to the form. 7 MR. LOCKE: Objection. 8 THE WITNESS: To me it's overly broad, 9 and I think that -- I think that if we go through 10 and we find a sentence or two in here that are 11 agreeable or not, there's a -- there's a much, 12 much bigger proposition here about what's going 13 on, and I don't think it boils down to any one of 14 these sentences. 15 And I think this looks like a passionate 16 opinion piece, right. That's calling it an 17 article, but it's a commentary. And, you know, 18 these guys might believe that, but I don't -- I 19 don't think it's a mainstream view, and it's not 20 my view, you know, without any qualifications 21 that -- that that statement is correct either. 22 Q Okay. Are you aware that over 800 23 statisticians and scientists signed on to this 24 document to push the concept of abandoning 25 statistical significance?</p>	<p style="text-align: right;">Page 308</p> <p>1 is that correct? 2 A I didn't. 3 MS. BROWN: Asked and answered. 4 BY MS. PARFITT: 5 Q All right. Now, let me have marked now 6 as Exhibit No. 19. 7 (Diette Exhibit No. 19 was marked 8 for identification.) 9 BY MS. PARFITT: 10 Q Do you have that, Doctor? 11 Take a look at that, if you will. 12 A (Peruses document.) So is this meant to 13 be a couple of things? 14 Q It's two things. I will represent to 15 you that the face sheet states "Johns Hopkins 16 Institute for Clinical and Translational 17 Research." The American Statistician special 18 issue, "Moving to a World Beyond P < 0.05." It's 19 dated March 25, 2019. It has The American 20 Statistician on the side. 21 A What are we -- I'm confused, though. 22 This is -- this is Exhibit 17 with something 23 attached to it or -- 24 Q You know, that's exactly it. And if you 25 look at Exhibit 19 --</p>
<p style="text-align: right;">Page 307</p> <p>1 MS. BROWN: Objection to the form. 2 MR. LOCKE: Objection. 3 THE WITNESS: I saw that. 4 BY MS. PARFITT: 5 Q Okay. You weren't one of those, were 6 you? 7 MS. BROWN: Objection to the form. 8 THE WITNESS: I'm not a statistician. 9 BY MS. PARFITT: 10 Q Okay. Well, but you use statistics in 11 your practice? 12 A I do. 13 Q Okay. Did anyone say you had to be a 14 statistician to sign on to that proposition? 15 A Well, I -- I thought I heard you say 16 statisticians. Maybe I -- I might have misheard. 17 I thought you said 800 statisticians. 18 Q I said there are about 800 statisticians 19 and other scientists that -- 20 A Oh, and other scientists. 21 Q -- yeah, that signed on to this. 22 A No, I didn't hear right. So I just -- 23 so I don't know what the criteria were for who 24 could sign or not sign. 25 Q Okay. You didn't sign on to it, though;</p>	<p style="text-align: right;">Page 309</p> <p>1 A Mm-hmm. 2 Q -- it is moving -- it states "Moving to 3 the World Beyond P" -- it's a special issue of The 4 American Statistician. The lead article calls for 5 abandoning the use of status -- statistically 6 significant, and offers much, not just one thing, 7 to replace it, written by Ron Wasserstein, Allen 8 Shirm, and Nicole Lazar. The coeditors of this 9 special issue summarize the content of the issue's 10 43 articles. 11 These articles -- and put this up 12 there -- discuss the use of p-values and 13 statistical significance that Johns Hopkins' 14 researchers may find beneficial, and it attaches 15 the full article, which is what's been marked as 16 Exhibit No. 17. 17 Do you see that? 18 A I do. 19 Q Okay. Did anyone share with you at 20 Johns Hopkins that their Clinical and 21 Translational Research group was disseminating the 22 article by Wasserstein, "Moving to a World Beyond 23 P < 0.05," and urging individuals not only to 24 abandon the use of statistical significance, but 25 to discuss the use of p-values and statistical</p>

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 310</p> <p>1 significance with the researchers at Johns 2 Hopkins? 3 And that's a mouthful. So let me make 4 it really clear. 5 MS. BROWN: Let me object -- 6 MS. PARFITT: I move to strike the 7 question. 8 MS. BROWN: You're going to strike it? 9 MS. PARFITT: Yeah, let me strike it. 10 BY MS. PARFITT: 11 Q Were you aware, Dr. Diette, that the 12 division of Clinical and Translational Research 13 over at Hopkins had distributed to its scientists 14 this group of 43 articles, including the 15 Wassertine -- Wasserstein, for purposes of 16 educating them with regard to this concern over 17 the misuse of statistical significance? 18 MS. BROWN: I object to a complete 19 misrepresentation of the exhibit and to 20 foundation. 21 THE WITNESS: So I mean, there's a lot 22 of things, right. I'll try to answer as many as I 23 can. 24 So one is that I probably got something 25 because I'm -- I've been part of the ICTR, and I</p>	<p style="text-align: right;">Page 312</p> <p>1 read all 800, but I looked to see if there were 2 people from Hopkins in particular that signed it, 3 and I knew one of the two. 4 Q Okay. Let me show you what we'll have 5 marked as Exhibit No. 20. And I will represent to 6 you that it is a list of the 800 signatories that 7 joined together to support this movement to 8 abandon p-value in statistical significance. 9 (Diette Exhibit No. 20 was marked 10 for identification.) 11 MS. PARFITT: Again, Counsel, I 12 apologize. Apparently, we only have one copy of 13 this document. 14 MS. BROWN: So is it the blog soliciting 15 the signatures, or is it just the list? 16 MS. PARFITT: It is the list of 17 signatories. 18 MS. BROWN: Okay, that's fine. 19 BY MS. PARFITT: 20 Q Do you see that? 21 A I do. 22 Q Okay. Do you know an Elizabeth Ogburn? 23 A I don't. I saw her name on here, but 24 I -- I don't know her. 25 Q All right. Do you know Daniel</p>
<p style="text-align: right;">Page 311</p> <p>1 use the resources, I'm one of the people who 2 helped to write the grant to get it funded, and 3 so -- like I get a zillion things that fly by. 4 I don't know if I saw this or not, but I 5 probably wouldn't have clicked on it if it came 6 through like an e-mail because I had already seen 7 it, like, as part of this -- as part of the Bowman 8 deposition. 9 BY MS. PARFITT: 10 Q Mm-hmm. 11 A But other than that, I mean, I think 12 it's -- I think they're smart to do it. They 13 should always put stuff out there for people to 14 read. It doesn't mean that we're going to get rid 15 of p of 0.05. It doesn't mean we're going to get 16 rid of statistical significance. They're just 17 saying it's an interesting read. 18 Q Do you know any of the signatories to 19 this particular document? 20 A I found one. One that I know 21 personally, and I'm just trying to remember if 22 there was anybody else that I saw. 23 Q Well, let me show you what we'll have 24 marked as Exhibit No. 20. 25 A Yeah, so let me just say, so I didn't</p>	<p style="text-align: right;">Page 313</p> <p>1 Sharfenstein (phonetic)? 2 A Sharfstein, and I know him. Yeah. 3 Q Okay. Is that -- do you know anyone 4 else that might appear on that list? 5 A I don't know. I didn't read it. I 6 just -- I literally just did a word search for 7 "Hopkins," and I came up with like one person 8 whose name is Hopkins who works in England, and 9 another one, something Hopkins Institute, which is 10 not, and then two from Johns Hopkins. 11 Q Okay. When did you do this research? 12 A In the last week. I mean, after -- 13 after reading the Bowman deposition. 14 Q All right. So you read the Bowman 15 deposition, and then you -- what caused you then 16 to -- to go back and look at that or for that? 17 A Well, because it sounds like an 18 interesting topic, and, you know, who knows, maybe 19 one day it either will or won't change, but it's 20 an interesting thing to read about. And so I 21 wanted to just sort of see what -- what you guys 22 were driving at. And then since I saw that there 23 were 800 signatories, I just figured I would see 24 if there was anybody at Hopkins that was part of 25 it or not.</p>

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 314</p> <p>1 Q Mm-hmm. And you found a couple of</p> <p>2 people from Hopkins?</p> <p>3 A Yeah, I found two. One I know, one I</p> <p>4 don't.</p> <p>5 Q All right. Again, you were not one of</p> <p>6 the signatories?</p> <p>7 A Still true, yeah.</p> <p>8 Q Okay. Okay. What position does</p> <p>9 Dr. Sharfstein hold within the University?</p> <p>10 MS. BROWN: Objection. Speculation.</p> <p>11 THE WITNESS: He's been in the</p> <p>12 Department of Biostatistics, and I don't know</p> <p>13 what -- what other ways to label what he -- what</p> <p>14 his positions are.</p> <p>15 BY MS. PARFITT:</p> <p>16 Q Okay. From the time you saw the</p> <p>17 discussion about statistical significance and a</p> <p>18 movement away from that and did your bit of</p> <p>19 research, did you ever call Dr. Sharfstein to talk</p> <p>20 to him about it?</p> <p>21 A Not yet. I'm hoping I'll just run into</p> <p>22 him at some point and -- and ask him about that.</p> <p>23 Q Is the -- is your interest strong enough</p> <p>24 that you might reach out to him?</p> <p>25 MS. BROWN: Objection to the form.</p>	<p style="text-align: right;">Page 316</p> <p>1 significance and p-values?</p> <p>2 A Yeah, well, I'd say the real world,</p> <p>3 right. And the real world --</p> <p>4 Q I'm sorry. You're in the real world?</p> <p>5 A Real world, yeah.</p> <p>6 Q Okay. And what's the real world doing?</p> <p>7 A Well, the real world, if I want to write</p> <p>8 a grant, I have to provide people with a sample</p> <p>9 size estimate of what it is that I'm looking for,</p> <p>10 and the sample size estimate is almost always</p> <p>11 based on hypothesis testing. And you have to</p> <p>12 declare a certain p-value that you find to be a</p> <p>13 credible one.</p> <p>14 So I can't just say, I've decided</p> <p>15 because I read some editorial that I'm not going</p> <p>16 to use a p-value of 0.05. That I'm still stuck</p> <p>17 with 0.05 as a -- as an estimate. And so if I</p> <p>18 want to have any success getting a grant, I'm</p> <p>19 going to have to still use the rules that we've</p> <p>20 used for years.</p> <p>21 And if I publish a paper, I happened to</p> <p>22 look because I thought it was curious, I went on</p> <p>23 New England Journal's website --</p> <p>24 Q Yes.</p> <p>25 A -- and they have an extensive list of</p>
<p style="text-align: right;">Page 315</p> <p>1 What -- what interest are we talking about?</p> <p>2 BY MS. PARFITT:</p> <p>3 Q Interest in this science that you have</p> <p>4 indicated yourself seems to be pretty important.</p> <p>5 MS. BROWN: Objection. That misstates</p> <p>6 his testimony by a lot.</p> <p>7 THE WITNESS: So it -- it might be. I</p> <p>8 mean, the -- the reason there's no urgency for me</p> <p>9 to do it is that I still live in the world in</p> <p>10 2019, and I'm still living in a world where</p> <p>11 hypothesis testing is the rule and p-values are</p> <p>12 part of what you're required to report if you're</p> <p>13 going to publish a paper in a credible journal.</p> <p>14 And so, you know, whether -- whether</p> <p>15 this gets traction or not, you know, we'll see. I</p> <p>16 don't know what the replacement is going to be. I</p> <p>17 don't know if chaos will ensue. It's an</p> <p>18 interesting topic to talk about, but it's sure not</p> <p>19 ready for prime time.</p> <p>20 So I think if I see Dan in the hall, I</p> <p>21 might ask him about it, but there's no -- there's</p> <p>22 no urgency to it.</p> <p>23 BY MS. PARFITT:</p> <p>24 Q So what's the world you're living in</p> <p>25 with regard to the relevance of statistical</p>	<p style="text-align: right;">Page 317</p> <p>1 ways in order to represent your p-values and your</p> <p>2 confidence intervals that you have to adhere to if</p> <p>3 you want to publish your papers. You know, Nature</p> <p>4 said that they're not going to change their rules</p> <p>5 based on this.</p> <p>6 So, anyway, so it's like it's -- that's</p> <p>7 the world that we live in right now. If you want</p> <p>8 to communicate about -- about clinical science,</p> <p>9 then you're going to have to use the rules that</p> <p>10 we've learned to -- that we've learned to use.</p> <p>11 Q Do you know if the rules you've just set</p> <p>12 forth are the rules that Dr. -- or, excuse me,</p> <p>13 that Dr. Rothman and Sander Greenland, esteemed</p> <p>14 epidemiologists, promote in their practice?</p> <p>15 A I have no idea what they promote.</p> <p>16 Q Well, you read the article in Nature,</p> <p>17 didn't you?</p> <p>18 A Yeah, but you said "their practice." I</p> <p>19 don't even know what that is even.</p> <p>20 Q Well, who is the author of the Nature</p> <p>21 article?</p> <p>22 A We're talking about the -- the</p> <p>23 commentary?</p> <p>24 Q That's right.</p> <p>25 A Yeah. So it looks like Armhein,</p>

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 318</p> <p>1 Greenland and McShane. Or maybe not. Maybe</p> <p>2 that's -- wait a minute, I could be wrong. No,</p> <p>3 it's -- it's those three.</p> <p>4 Q And again, you don't know -- do you know</p> <p>5 any of them? I know you don't know Dr. Greenland.</p> <p>6 Do you know any of the others?</p> <p>7 A I do not.</p> <p>8 Q Okay. So if I understand your opinion</p> <p>9 today, you still believe in the strength of a</p> <p>10 statistical significance versus not statistically</p> <p>11 significant?</p> <p>12 A It's --</p> <p>13 MS. BROWN: Objection to the form.</p> <p>14 THE WITNESS: It's still a factor to</p> <p>15 consider when either planning, conducting, or</p> <p>16 interpreting a study.</p> <p>17 BY MS. PARFITT:</p> <p>18 Q Okay. And do you still live in the</p> <p>19 world that there is a threshold of a p-value of</p> <p>20 0.05?</p> <p>21 A It depends.</p> <p>22 Q Well, what do you mean "it depends"?</p> <p>23 A I'm going to explain.</p> <p>24 Q Please.</p> <p>25 A So that's why I used the example of p at</p>	<p style="text-align: right;">Page 320</p> <p>1 took wasn't anything novel or different. I mean,</p> <p>2 I don't know at all what his plans are going</p> <p>3 forward, but he still works at the University</p> <p>4 where we still compete for NIH grants --</p> <p>5 Q Mm-hmm.</p> <p>6 A -- and I haven't seen any change in the</p> <p>7 NIH's posture on this, and I haven't seen any, you</p> <p>8 know, ground swell of support for just doing</p> <p>9 whatever you feel like in order to publish your</p> <p>10 paper.</p> <p>11 Q Well, are you suggesting that what</p> <p>12 Dr. Greenland and others and Dr. Wasserstein have</p> <p>13 suggested to do whatever you -- let me get your</p> <p>14 words -- shall -- yeah. Okay.</p> <p>15 MS. PARFITT: Tell you what, let's take</p> <p>16 a quick break. I want to find that part, and</p> <p>17 we'll get back. Let's take a quick break.</p> <p>18 THE VIDEOGRAPHER: The time is 2:44 p.m.</p> <p>19 We're going off the record.</p> <p>20 (Recess.)</p> <p>21 THE VIDEOGRAPHER: The time is 2:53</p> <p>22 p.m., and we're back on the record.</p> <p>23 BY MS. PARFITT:</p> <p>24 Q Dr. Diette, when we left just before the</p> <p>25 break, you said: "I haven't seen any ground swell</p>
<p style="text-align: right;">Page 319</p> <p>1 0.05, right? I could just say, I have decided</p> <p>2 that now I only want to do studies with six people</p> <p>3 in them, and I'll be happy to have a p-value of</p> <p>4 0.5. You'd have to wish me luck getting it</p> <p>5 published anywhere because it's not going to</p> <p>6 happen, right?</p> <p>7 So if I still want to do research and I</p> <p>8 still want to get it published, I'm going to have</p> <p>9 to pick a threshold for a p-value that's agreeable</p> <p>10 to the peer reviewers and to the editor. And it</p> <p>11 doesn't have to be 0.05. In some circumstances it</p> <p>12 might be 0.01. It might be even lower than that.</p> <p>13 But a -- but a p threshold is necessary, at least</p> <p>14 in our current era, if you want to be able to</p> <p>15 conduct and talk about your research.</p> <p>16 Q Do you -- do you think Dr. Sharfstein is</p> <p>17 going to now have difficulty having his scientific</p> <p>18 works published?</p> <p>19 MS. BROWN: Objection. Based on what?</p> <p>20 There's no foundation for that question.</p> <p>21 BY MS. PARFITT:</p> <p>22 Q You can answer the question, Doctor.</p> <p>23 A Well, exactly that. So -- so Sharfstein</p> <p>24 has been involved in some of our research and some</p> <p>25 critical illness stuff, and the approach that we</p>	<p style="text-align: right;">Page 321</p> <p>1 of support for doing whatever you feel like in</p> <p>2 order to publish your paper."</p> <p>3 I'm not talking about the publication of</p> <p>4 papers. What I would like to know from you is, do</p> <p>5 you agree, though, when you were evaluating the</p> <p>6 consistency of evidence, that one should not</p> <p>7 disregard studies that are nonstatistically</p> <p>8 significant and give greater weight to those that</p> <p>9 are statistically significant?</p> <p>10 MS. BROWN: Objection to the form of the</p> <p>11 question.</p> <p>12 THE WITNESS: I hear two questions</p> <p>13 there, and the first part I agree with, and the</p> <p>14 second part, it depends.</p> <p>15 BY MS. PARFITT:</p> <p>16 Q Okay. Do you agree that when you are</p> <p>17 evaluating and weighing evidence, studies, that</p> <p>18 you should evaluate studies the same whether they</p> <p>19 are statistically significant or not statistically</p> <p>20 significant?</p> <p>21 MS. BROWN: Objection to the form. In</p> <p>22 what context?</p> <p>23 THE WITNESS: I don't know what</p> <p>24 "evaluate the same" means. I mean, I think any --</p> <p>25 any study that you think should be evaluated</p>

81 (Pages 318 to 321)

Gregory B. Diette, M.D.

Page 322	Page 324
<p>1 should be evaluated, you know, as thoroughly as</p> <p>2 you can.</p> <p>3 BY MS. PARFITT:</p> <p>4 Q When you're evaluating the consistency</p> <p>5 of studies, is it proper epidemiology to consider</p> <p>6 those studies whether or not they are</p> <p>7 statistically significant or nonstatistically</p> <p>8 significant?</p> <p>9 MS. BROWN: Objection to the form.</p> <p>10 THE WITNESS: It is. And I think, you</p> <p>11 know, regardless of what Dr. Rothman has written,</p> <p>12 you know, it's part of the information that's</p> <p>13 available to you, and I think to ignore it would</p> <p>14 be, you know, not in your best interest.</p> <p>15 BY MS. PARFITT:</p> <p>16 Q Okay. And would you agree that one</p> <p>17 should not conclude there is no association or no</p> <p>18 difference just because a -- one study is</p> <p>19 statistically significant and another study is</p> <p>20 significant?</p> <p>21 MS. BROWN: Objection to the form.</p> <p>22 THE WITNESS: And I agree with you,</p> <p>23 especially because you used "just because."</p> <p>24 BY MS. PARFITT:</p> <p>25 Q All right. So maybe -- what do you</p>	<p>1 BY MS. PARFITT:</p> <p>2 Q Okay. Now, let's turn to -- your chart,</p> <p>3 and specifically the studies that you set forth in</p> <p>4 your report on pages 13 and 14.</p> <p>5 And if you'd go to your report, 13 and</p> <p>6 14.</p> <p>7 A I'm sorry, I've got somebody else's</p> <p>8 thing here.</p> <p>9 Q That's okay.</p> <p>10 A Okay.</p> <p>11 Q Okay. You got there? All right.</p> <p>12 What I would like -- all right. So you</p> <p>13 have that in front of you, correct, sir?</p> <p>14 A I do.</p> <p>15 Q Okay. Now, what I'll have marked as --</p> <p>16 for demonstrative purposes is a chart that we have</p> <p>17 marked as Diette Exhibit 21.</p> <p>18 (Diette Exhibit No. 21 was marked</p> <p>19 for identification.)</p> <p>20 BY MS. PARFITT:</p> <p>21 Q And let me hand that to you.</p> <p>22 MS. BROWN: Counsel, can you give a</p> <p>23 representation for the record about what</p> <p>24 Exhibit 21 is?</p> <p>25 MS. PARFITT: Yes, I was about to do</p>
Page 323	Page 325
<p>1 mean?</p> <p>2 A No, it's a good sentence. I mean, I --</p> <p>3 it -- I think that over and over what we're</p> <p>4 talking about is that -- that you shouldn't be</p> <p>5 wedded to the idea that statistical significance</p> <p>6 is the only feature that you look at, but it</p> <p>7 doesn't mean that you don't look at it.</p> <p>8 And so when you say that, you know, if</p> <p>9 you were just to hold up two studies, and one was</p> <p>10 significant and the other one wasn't and -- that</p> <p>11 wouldn't -- you know, you wouldn't be curious</p> <p>12 enough. You would need to know more about those</p> <p>13 studies to reach the conclusion you do.</p> <p>14 So I think, you know, looking at the</p> <p>15 whole study, looking how it's built, looking how</p> <p>16 it's interpreted, all that's important.</p> <p>17 Q All right. So it would not be proper to</p> <p>18 conclude the two studies conflict just because one</p> <p>19 was significant and one was statistically</p> <p>20 significant.</p> <p>21 MS. BROWN: Objection. Misstates</p> <p>22 testimony.</p> <p>23 THE WITNESS: It -- not -- not by</p> <p>24 itself, but that is at least one indicator of</p> <p>25 something that's different about those studies.</p>	<p>1 that.</p> <p>2 MS. BROWN: Thank you.</p> <p>3 BY MS. PARFITT:</p> <p>4 Q Dr. Diette, on pages 13 and 14, you</p> <p>5 have -- of your report, you have listed I believe</p> <p>6 25 case-control studies, 3 cohort studies and --</p> <p>7 is that correct?</p> <p>8 MR. LOCKE: Objection.</p> <p>9 BY MS. PARFITT:</p> <p>10 Q You've got 7 population studies on the</p> <p>11 back. That's on page 14. You have 25</p> <p>12 case-control -- hospital studies, rather, on</p> <p>13 page 14, and 25 studies on page 13. Is that</p> <p>14 correct?</p> <p>15 MR. LOCKE: Do you have a copy for --</p> <p>16 MS. PARFITT: Beg your pardon?</p> <p>17 MR. LOCKE: Do you have a copy for me,</p> <p>18 please?</p> <p>19 MS. PARFITT: Oh, Tom, I think we do,</p> <p>20 yeah.</p> <p>21 MR. LOCKE: Thank you. Is this a --</p> <p>22 does this come from a published --</p> <p>23 MS. PARFITT: No. Let me represent --</p> <p>24 no, let me represent that Exhibit No -- Exhibit 21</p> <p>25 is a demonstrative which lists all of the studies</p>

82 (Pages 322 to 325)

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 326</p> <p>1 that Dr. Diette listed in his report on page 13 2 and 14 and has put them on a graph. 3 MS. BROWN: Who -- who put them on a 4 graph and what is the graph? 5 MS. PARFITT: Counsel -- 6 MS. BROWN: Well, I'm going to have an 7 objection to this document, and I just want to -- 8 MS. PARFITT: You can. You can object 9 to this -- 10 MS. BROWN: -- make sure I'm properly 11 objecting, because I don't know what it is, who 12 made it, based on what, and to the extent the 13 doctor needs the underlying studies to answer your 14 questions. We'll -- 15 MS. PARFITT: Counsel, no speaking 16 objections. 17 MS. BROWN: I just want to object to 18 this. 19 BY MS. PARFITT: 20 Q Dr. Diette -- 21 MS. PARFITT: I understand, Counsel. I 22 know what you're doing. 23 MS. BROWN: The name is Diette. 24 MS. PARFITT: Diette? 25 MS. BROWN: Diette.</p>	<p style="text-align: right;">Page 328</p> <p>1 MS. PARFITT: Yeah, there you go. 2 There you go, Doctor. 3 BY MS. PARFITT: 4 Q Doctor, I've handed you what's marked as 5 Exhibit 22. It is the -- an article by Patricia 6 Hartge dated 1983 in JAMA. Do you see that? 7 A I do. 8 Q Okay. And at the top of the study, she 9 has a table entitled "Estimated Relative Risk." 10 Do you see that? 11 A I do. 12 Q And I'll put this up on the ELMO. 13 MS. PARFITT: Okay. And it's hard to 14 see. We'll have to zero in there. There you go. 15 Okay. 16 BY MS. PARFITT: 17 Q You'll see on your chart you had listed 18 for Hartge, 1983, a relative risk of 0.7 with a 19 confidence interval of 0.40 to 1.10. 20 Do you see that? 21 A Uh -- 22 Q Look at your -- 23 A I do, yep. 24 Q -- on page 14. 25 Okay. Now, look at the table of the</p>
<p style="text-align: right;">Page 327</p> <p>1 MS. PARFITT: Diette. 2 BY MS. PARFITT: 3 Q I'm sorry, Dr. Diette. I'm not doing it 4 to annoy you. 5 A You've had it -- you've had it right all 6 day. You're good. 7 Q Thank you. Thank you. I appreciate 8 that. 9 What I will represent to you, and you 10 can track it, Dr. Diette, that Exhibit No. 21 11 represents the sales studies you selected for 12 purposes of your expert report. It lists them 13 study by study. It plots them on a forest plot on 14 the right-hand side. 15 Do you see that? 16 A I do. 17 Q Okay. And I'll represent that we took 18 your relative risks and confidence intervals, and 19 simply extracted those and put them on Exhibit 21 20 with one exception. 21 What I'd like you to do is look at 22 Hartge. And we will have that marked as 23 Exhibit 22. 24 (Diette Exhibit No. 22 was marked 25 for identification.)</p>	<p style="text-align: right;">Page 329</p> <p>1 Hartge study under "Genital Talc Use." 2 Do you see that? 3 A I do. 4 Q Okay. And do you see where Dr. Hartge 5 reports that the relative risk for genital use 6 talcum powder is not what you have as 0.7, but 2.5 7 with a confidence interval of 0.7 to 10. 8 Do you see that? 9 A I do. 10 Q All right. So that would be an error in 11 your chart; is that correct? 12 MS. BROWN: Objection. 13 Doctor, take as long as you need to look 14 at what counsel is asking you about. 15 And -- 16 MS. PARFITT: Counsel -- 17 MS. BROWN: -- Counsel, do you mean 18 to -- 19 MS. PARFITT: Counsel -- 20 MS. BROWN: -- misrepresent the 21 paragraph? 22 MS. PARFITT: No, Counsel. And, listen, 23 if the Doctor doesn't have any questions -- he's a 24 very intelligent man as we've seen today -- 25 MS. BROWN: I know, but what you're</p>

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 330</p> <p>1 saying is not right.</p> <p>2 MS. PARFITT: Counsel, that's it. No.</p> <p>3 I'm sorry.</p> <p>4 MS. BROWN: Are you intentionally</p> <p>5 misrepresenting what's in the paper?</p> <p>6 MS. PARFITT: Counsel, if you heard my</p> <p>7 question -- I think Dr. Diette understands the</p> <p>8 question.</p> <p>9 BY MS. PARFITT:</p> <p>10 Q Dr. Diette, we have on the table a</p> <p>11 genital use, which is 2.5 with a confidence</p> <p>12 interval of 0.7 to 10.</p> <p>13 Do you see that?</p> <p>14 A Yeah, I'm sorry. Can you give me just</p> <p>15 one second?</p> <p>16 Q Okay. Of course I can.</p> <p>17 A Thank you. (Peruses document.)</p> <p>18 Yeah, I'm with you.</p> <p>19 Q Okay. And the only correction I -- I</p> <p>20 wish to make is that, instead of the 0.70 that you</p> <p>21 have for Hartge, it should be 2.5 --</p> <p>22 MS. BROWN: Objection.</p> <p>23 BY MS. PARFITT:</p> <p>24 Q -- for the genital --</p> <p>25 MS. PARFITT: Let me finish, Counsel.</p>	<p style="text-align: right;">Page 332</p> <p>1 MS. BROWN: Okay. Then let him --</p> <p>2 MS. PARFITT: I just don't want you</p> <p>3 coaching --</p> <p>4 MS. BROWN: -- answer the question.</p> <p>5 MS. PARFITT: -- and touching the paper</p> <p>6 and pointing at things.</p> <p>7 MS. BROWN: You are intentionally</p> <p>8 misreading this document.</p> <p>9 BY MS. PARFITT:</p> <p>10 Q Doctor -- all right, Dr. Diette, you're</p> <p>11 the one I'm interested in hearing from, to be</p> <p>12 perfectly candid.</p> <p>13 My question is, are the -- is the</p> <p>14 relative risk that you have listed for Hartge</p> <p>15 0.70, or should it be 2.5?</p> <p>16 A You know, the -- the study report is</p> <p>17 really tough I think to decide that either one of</p> <p>18 them is ideal. And for a couple of reasons, and</p> <p>19 one is just because this -- this genital with an</p> <p>20 asterisk, it isn't literally just genital</p> <p>21 application. It includes sanitary napkins.</p> <p>22 And you can see in a lot of the studies</p> <p>23 that people have sort of broken out sanitary</p> <p>24 napkin use separate from like perineal</p> <p>25 application.</p>
<p style="text-align: right;">Page 331</p> <p>1 BY MS. PARFITT:</p> <p>2 Q -- for the genital use of talc. Do you</p> <p>3 agree with that?</p> <p>4 MS. BROWN: Objection to the form.</p> <p>5 THE WITNESS: So, maybe. I'm just</p> <p>6 trying to think about how I got --</p> <p>7 BY MS. PARFITT:</p> <p>8 Q Sure.</p> <p>9 A -- got here. Because the -- you know,</p> <p>10 the text says that it's -- there were ten users,</p> <p>11 so I guess like seven cases and three controls.</p> <p>12 Q Mm-hmm.</p> <p>13 A It said -- specifically mentioned use on</p> <p>14 sanitary napkins, underwear, or the genital area.</p> <p>15 But then it says -- but estimated is</p> <p>16 2.5, but the small number of exposed women yielded</p> <p>17 an unreliable estimate. So I --</p> <p>18 MS. BROWN: It's --</p> <p>19 THE WITNESS: Yeah --</p> <p>20 MS. PARFITT: You don't have to show the</p> <p>21 doctor.</p> <p>22 MS. BROWN: Do you want the truth on the</p> <p>23 record, or do you want --</p> <p>24 MS. PARFITT: You know, I really do want</p> <p>25 the truth.</p>	<p style="text-align: right;">Page 333</p> <p>1 And so, you know, that's not an ideal</p> <p>2 measure for this -- this chart either. I mean, I</p> <p>3 get your point, the all over is something else.</p> <p>4 But there's at least -- you know, there's more</p> <p>5 than ten people at least in that particular --</p> <p>6 that particular row. So I -- I'm not sure if</p> <p>7 either of these is great, but they --</p> <p>8 Q Well, the analysis you went through, did</p> <p>9 you go through that analysis for each and every</p> <p>10 one of the studies that you listed when you made a</p> <p>11 decision as to which odds ratio to select?</p> <p>12 A I did.</p> <p>13 Q You did.</p> <p>14 A I mean, I tried to pick the one that --</p> <p>15 that fit the best.</p> <p>16 Q Okay. And is the one that fits the best</p> <p>17 for Hartge the 0.70, or is the one that fits the</p> <p>18 best for Hartge the 2.5?</p> <p>19 MS. BROWN: Objection to the form.</p> <p>20 THE WITNESS: So I don't know. I mean</p> <p>21 other than the fact that you've got the word</p> <p>22 "genital" there, I mean "all over" is kind of</p> <p>23 confusing, right, because it doesn't say like "all</p> <p>24 over except the genitals," right.</p> <p>25 And so that's where it gets kind of</p>

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 334</p> <p>1 confusing is how you -- it's not a great study, 2 right. I mean, I'm not saying the study is not 3 great. I'm saying the report of the study doesn't 4 really tell us everything that you could really 5 wish to know. 6 BY MS. PARFITT: 7 Q So would you like to keep your chart 8 with the 0.70, or do you think the chart should be 9 modified to say 2.5? 10 MS. BROWN: Objection to the form. 11 THE WITNESS: I mean, I'd be happy to 12 put both rows there and just with an asterisk, and 13 explain, you know, what each one of those is. 14 BY MS. PARFITT: 15 Q Okay. Would you -- have you done that 16 for all the other studies that you've listed here, 17 wherein there may be data for sanitary napkins and 18 data for genital use and data for cornstarch? Did 19 you go through that analysis? 20 MS. BROWN: Objection to the form. 21 THE WITNESS: So, for this table I 22 haven't, but I have gone through all the sanitary 23 napkin findings that I can. And that's one of the 24 things you'll find in my handwritten notes from 25 the -- from the prior case.</p>	<p style="text-align: right;">Page 336</p> <p>1 you did, where is that contained in your report? 2 MS. BROWN: And you should feel free to 3 answer both questions since counsel cut you off. 4 THE WITNESS: I have no idea about what 5 you mean by where it is in the report. 6 BY MS. PARFITT: 7 Q Well, I only have RRs here. I have a 8 table. No analyses of the different case 9 controls. Just a table of their relative risks. 10 So, you've now gone through an analysis 11 of the Hartge case and said, You know, maybe this 12 is what we should have extracted, maybe we should 13 have looked at this, but I used my judgment and 14 put the 0.7. 15 And what I'm asking is, is that analyses 16 that you just did for us on the record the kind of 17 analysis that you did for all the other studies? 18 And if it was, where in the 51 pages of your 19 report or this chart have you included that 20 information? 21 MS. BROWN: Objection. Completely 22 misstates his testimony, as well as the article, 23 as well as the report, as well as the chart. 24 THE WITNESS: Let me just see. So 25 obviously it's not -- it's not documented, but I</p>
<p style="text-align: right;">Page 335</p> <p>1 In terms of cornstarch, that's a 2 different question. 3 BY MS. PARFITT: 4 Q And, Doctor, I -- 5 MS. BROWN: Wait, he needs to finish. 6 He's got to -- 7 BY MS. PARFITT: 8 Q Doctor, that's really not my question. 9 MS. BROWN: No, no, no, no, no, he -- 10 BY MS. PARFITT: 11 Q My question is this -- 12 MS. BROWN: Counsel. 13 MS. PARFITT: Counsel. 14 BY MS. PARFITT: 15 Q My question is -- 16 MS. BROWN: He has to finish the 17 question. 18 BY MS. PARFITT: 19 Q You're not answering my question. Mine 20 is a very simple one. 21 My question was -- if you'll be patient 22 with me, my question was: The analysis that 23 you've just talked about that you're going through 24 with Hartge, did you go through a similar analysis 25 for each and every one of these studies; and if</p>	<p style="text-align: right;">Page 337</p> <p>1 think part of what I'm trying to do is communicate 2 what the -- what the risks are that were reported 3 and what their confidence bounds were. 4 And so, you know, the papers stand for 5 themselves. They all exist. They're all cited. 6 We can look at anything we want. 7 I think in terms of the cornstarch 8 issue -- 9 BY MS. PARFITT: 10 Q Doctor, I'm not asking about -- 11 MS. BROWN: Stop cutting him off. 12 BY MS. PARFITT: 13 Q -- the cornstarch. We can talk about 14 that later. I'm not talking about cornstarch. 15 MS. BROWN: You cannot continue to cut 16 him off, or we'll have to call the Judge. 17 MS. PARFITT: I don't have a question 18 about cornstarch. 19 MS. BROWN: He's answering your 20 question. 21 MS. PARFITT: He is not. 22 MS. BROWN: You have to let him answer 23 or we have to call the Judge. You are 24 violating -- 25 MS. PARFITT: You can do it in your</p>

85 (Pages 334 to 337)

Gregory B. Diette, M.D.

Page 338	Page 340
<p>1 direct.</p> <p>2 MS. BROWN: No, you have to let him</p> <p>3 answer the question or --</p> <p>4 MS. PARFITT: Counsel.</p> <p>5 MS. BROWN: We're going off the record.</p> <p>6 MS. PARFITT: Do you want to go -- we'll</p> <p>7 go off the record right now.</p> <p>8 MS. BROWN: Yeah, let's go. Fine. Do</p> <p>9 we need to call the Judge? You have to let him</p> <p>10 answer.</p> <p>11 MS. PARFITT: We'll call her. We'll</p> <p>12 call her.</p> <p>13 THE VIDEOGRAPHER: The time is 3:09 p.m.</p> <p>14 We're going off the record.</p> <p>15 (A discussion was held off the record.)</p> <p>16 THE VIDEOGRAPHER: The time is</p> <p>17 3:10 p.m., and we're back on the record.</p> <p>18 MS. PARFITT: Thank you.</p> <p>19 BY MS. PARFITT:</p> <p>20 Q And, Dr. Diette, all I'm trying to -- to</p> <p>21 ask, and obviously very poorly, is the analysis</p> <p>22 that you just discussed that you went through with</p> <p>23 Hartge, as we sat here today and you did it on the</p> <p>24 record, did you do that for all the other studies?</p> <p>25 A I tried to.</p>	<p>1 BY MS. PARFITT:</p> <p>2 Q Correct?</p> <p>3 A I did.</p> <p>4 Q Okay. And my last question is, is that</p> <p>5 the position you wish to take today?</p> <p>6 MS. BROWN: Objection to the form.</p> <p>7 BY MS. PARFITT:</p> <p>8 Q Or would you modify that and use a</p> <p>9 different relative risk? That's all.</p> <p>10 A I don't --</p> <p>11 MS. BROWN: Objection.</p> <p>12 THE WITNESS: I don't think anybody is</p> <p>13 well served by looking at this other number, other</p> <p>14 than if you're just trying to make a point and</p> <p>15 be -- you know, for a plaintiff or something to</p> <p>16 look at this 2.5.</p> <p>17 I think if you take this one that says</p> <p>18 there's a small number of exposed women, ten</p> <p>19 people, you know, that yields an unreliable</p> <p>20 estimate. I mean, somebody should fuss about that</p> <p>21 too. So that's not -- that's not an ideal</p> <p>22 measure.</p> <p>23 If it helps, we can put them on the</p> <p>24 table, and it wouldn't really change things,</p> <p>25 right. You've got confidence bounds from 0.7 to</p>
Page 339	Page 341
<p>1 Q Okay. And so you had to make</p> <p>2 determinations as to what relative risks to</p> <p>3 extract from those studies, correct?</p> <p>4 MS. BROWN: Objection to the form.</p> <p>5 THE WITNESS: I -- I had to work with</p> <p>6 what they reported.</p> <p>7 BY MS. PARFITT:</p> <p>8 Q Okay. And just like Hartge, they</p> <p>9 reported different pieces of information:</p> <p>10 Diaphragms used, no diaphragm, all over, genital,</p> <p>11 legs, feet, correct?</p> <p>12 A Correct.</p> <p>13 Q And you had to decide what was the most</p> <p>14 appropriate data to pull from those studies to</p> <p>15 include on your chart for relative risks, correct?</p> <p>16 A For the most --</p> <p>17 MS. BROWN: Objection to the form.</p> <p>18 THE WITNESS: Yes, of course.</p> <p>19 BY MS. PARFITT:</p> <p>20 Q Okay. So my question to you is, you</p> <p>21 chose for the Hartge, based upon that analysis, to</p> <p>22 use the -- any talc mentioned, which gave us a</p> <p>23 relative risk of 0.7, as opposed to genital, which</p> <p>24 would have represented a 2.5 risk.</p> <p>25 MS. BROWN: Objection to the form.</p>	<p>1 10. I mean, that's an enormous confidence value.</p> <p>2 So there's not a lot of information from those ten</p> <p>3 people.</p> <p>4 BY MS. PARFITT:</p> <p>5 Q And the reason I ask as well, as you</p> <p>6 said earlier on in your deposition, you did not</p> <p>7 know for all these studies their sample size.</p> <p>8 A Oh, no, no, no. I didn't memorize it,</p> <p>9 but I've got all the studies, and it's a piece of</p> <p>10 cake, we can just go look at them and look at the</p> <p>11 sample size. I didn't want to, like -- I didn't</p> <p>12 want to, like, make -- this is already a long</p> <p>13 enough report. I don't need to put every bit of</p> <p>14 data from every study in it to have it make sense</p> <p>15 to me.</p> <p>16 Q So somewhere you have all the sample</p> <p>17 sizes pulled together for the various cases and</p> <p>18 controls for each one of these studies?</p> <p>19 A It's in every one of the studies.</p> <p>20 Q I know it's in each and every one of the</p> <p>21 studies, but did you document it on any kind of</p> <p>22 chart or anything like that?</p> <p>23 A For what?</p> <p>24 Q So that you could tell someone like me</p> <p>25 and the Court why you chose the data that you did.</p>

86 (Pages 338 to 341)

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 342</p> <p>1 A We can just look at the studies. If I</p> <p>2 documented the sample size next to each one of</p> <p>3 these, it wouldn't tell you why I picked this</p> <p>4 particular relative risk.</p> <p>5 Q It would -- it would not offer valid</p> <p>6 information as to the relevance of those relative</p> <p>7 risks?</p> <p>8 A Oh, my gosh. I mean if you were</p> <p>9 interested in it, I could find it for you. It</p> <p>10 wasn't -- it wasn't important for me to</p> <p>11 communicate what I was trying to communicate.</p> <p>12 Q No, I -- it's a different question.</p> <p>13 Is sample size important when one is</p> <p>14 doing an analysis of a scientific study?</p> <p>15 A Yeah, that's why it's in the paper.</p> <p>16 Q Okay. Because if the sample size is too</p> <p>17 small, it may be underpowered; is that correct?</p> <p>18 MS. BROWN: Objection.</p> <p>19 THE WITNESS: Well, I don't know. I</p> <p>20 mean, if we're going to do power now, I think</p> <p>21 that's going to be a different -- a different</p> <p>22 conversation.</p> <p>23 The sample size being small can have all</p> <p>24 kinds of -- all kinds of impact. This to me is</p> <p>25 actually the most generous way to look at these</p>	<p style="text-align: right;">Page 344</p> <p>1 doesn't change anything about this exercise.</p> <p>2 BY MS. PARFITT:</p> <p>3 Q Okay. Well, I didn't select Hartge.</p> <p>4 You selected Hartge.</p> <p>5 A Well, I selected it because it exists.</p> <p>6 I mean, I -- my -- my goal was to find all the</p> <p>7 studies that exist.</p> <p>8 Q Okay.</p> <p>9 A I mean, I didn't invent it, right? I</p> <p>10 just -- I just looked at --</p> <p>11 Q Well, I just didn't want the record to</p> <p>12 reflect that I was selecting your data.</p> <p>13 A No, but you -- it sounds like you would</p> <p>14 prefer me to use that 2.5 from the ten people,</p> <p>15 instead of the 0.7 from the nearly hundred people.</p> <p>16 Q I have --</p> <p>17 A And I'm happy to look at them both. I</p> <p>18 mean they both tell us some information. It's not</p> <p>19 like, you know, one is ideal and the other isn't.</p> <p>20 But it really doesn't change the basic premise</p> <p>21 here.</p> <p>22 Q All right. So on my chart I have them</p> <p>23 both. I have 0.7 and 2.5. Do you see that?</p> <p>24 A Um --</p> <p>25 Q Right at the bottom there, "Genital use"</p>
<p style="text-align: right;">Page 343</p> <p>1 data, rather than picking at the same size. I</p> <p>2 mean, I can do that too, right? I can say, This</p> <p>3 is a crummy study because it's got 23 people, or</p> <p>4 this is crummy one -- that wasn't my goal. It</p> <p>5 wasn't to sort of tear down the -- the</p> <p>6 case-control studies.</p> <p>7 I was trying to have a balanced approach</p> <p>8 here, I think unlike the plaintiffs' experts, and</p> <p>9 I wasn't trying to say that this one particular</p> <p>10 design is awful and the other one is good. I was</p> <p>11 just trying to represent something about it in</p> <p>12 order to summarize it and communicate a point.</p> <p>13 BY MS. PARFITT:</p> <p>14 Q Okay. And your balanced approach was to</p> <p>15 take the lower, the 0.7 relative risk, rather than</p> <p>16 the 2.5 relative risk.</p> <p>17 A Oh, my goodness.</p> <p>18 MS. BROWN: Objection to the form.</p> <p>19 THE WITNESS: I -- I think -- I mean, I</p> <p>20 think this little article, that doesn't even fit</p> <p>21 on an entire page, gives us so little information</p> <p>22 about what to do, and I think my point about there</p> <p>23 being ten people that provide a relatively</p> <p>24 uninformative risk, it's not great. If you want</p> <p>25 to use it, you're welcome to, but it doesn't -- it</p>	<p style="text-align: right;">Page 345</p> <p>1 and "Any talc use." Do you see that?</p> <p>2 A I do.</p> <p>3 Q Okay. All right. So as I appreciate</p> <p>4 your testimony, you had selected 25 population</p> <p>5 case controls, 7 hospital -- and 7 hospital case</p> <p>6 controls, correct?</p> <p>7 MS. BROWN: Objection.</p> <p>8 BY MS. PARFITT:</p> <p>9 Q Do I have the numbers right?</p> <p>10 A I wasn't listening. I'm sorry.</p> <p>11 MS. BROWN: Look at the realtime. I</p> <p>12 just think you misspoke. You said seven hospitals</p> <p>13 twice. Is that what you meant?</p> <p>14 BY MS. PARFITT:</p> <p>15 Q As I appreciate your testimony, you</p> <p>16 selected -- no, this is populate -- 25 population</p> <p>17 case controls and 7 hospital case controls. I</p> <p>18 said it twice. Correct?</p> <p>19 A That's correct.</p> <p>20 Q Okay. And that formed the basis for</p> <p>21 your selection of case studies, correct?</p> <p>22 MS. BROWN: Objection to the form.</p> <p>23 THE WITNESS: Case-control studies.</p> <p>24 BY MS. PARFITT:</p> <p>25 Q Case-control studies.</p>

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 346</p> <p>1 A Correct.</p> <p>2 Q Yes. Okay.</p> <p>3 Now, looking at the chart, which is 21,</p> <p>4 what is the point estimate -- wait.</p> <p>5 What I would like you to do, rather, I</p> <p>6 would like you to circle the point estimate for</p> <p>7 every study that exceeds -- that has a 1.0.</p> <p>8 MS. BROWN: Objection. Based on the</p> <p>9 document you created as 21?</p> <p>10 MS. PARFITT: Which is identical to the</p> <p>11 doctor's document, with the exception of I put two</p> <p>12 numbers for Hartge.</p> <p>13 MS. BROWN: You put two numbers for</p> <p>14 Moorman too.</p> <p>15 MS. PARFITT: Before and after 2014,</p> <p>16 correct?</p> <p>17 MS. BROWN: Nope, Moorman is 2009. You</p> <p>18 have -- you've broken out Moorman by race.</p> <p>19 MS. PARFITT: I did.</p> <p>20 MS. BROWN: So I mean, my point here is</p> <p>21 just if you wanted to use his report, he's happy</p> <p>22 to answer your questions, but --</p> <p>23 MS. PARFITT: He did it -- but he did it</p> <p>24 too.</p> <p>25 MS. BROWN: Okay. That's fine.</p>	<p style="text-align: right;">Page 348</p> <p>1 to be hard for me to read it off of your figure</p> <p>2 because I don't know, like -- like, the Harlow and</p> <p>3 Weiss one -- what is wrong with that one? Or is</p> <p>4 it --</p> <p>5 MS. BROWN: That looks wrong, doesn't</p> <p>6 it?</p> <p>7 THE WITNESS: No, it's Harlow and Weiss</p> <p>8 versus Harlow.</p> <p>9 So what am I circling? I'm circling</p> <p>10 the -- the -- on the forest plot?</p> <p>11 BY MS. PARFITT:</p> <p>12 Q On the forest plot, if you would be kind</p> <p>13 enough to circle every relative risk where the</p> <p>14 point estimate was 1.0 or above.</p> <p>15 A Oh, I did it wrong.</p> <p>16 Q That's all right.</p> <p>17 A Sorry. I'm circling the ones that</p> <p>18 are -- do you have another -- another copy of</p> <p>19 this?</p> <p>20 MS. MILLER: You can have mine.</p> <p>21 MR. LOCKE: I didn't --</p> <p>22 MS. PARFITT: I'm sorry. I'm sorry,</p> <p>23 Tom?</p> <p>24 MR. LOCKE: I just couldn't hear -- you</p> <p>25 trailed off at the end.</p>
<p style="text-align: right;">Page 347</p> <p>1 MS. PARFITT: It's on his chart.</p> <p>2 BY MS. PARFITT:</p> <p>3 Q I didn't do anything -- the only</p> <p>4 modification I made to your chart, Doctor, is</p> <p>5 Hartge, and there I kept your 0.70 and added the</p> <p>6 genital 2.5.</p> <p>7 And what I'd like you to do is circle in</p> <p>8 that document every point estimate or odds ratio</p> <p>9 that is 1.0 or above.</p> <p>10 A 1.0 or higher?</p> <p>11 Q That's right.</p> <p>12 MS. BROWN: Objection to the exercise.</p> <p>13 And, Doctor, if you need the articles,</p> <p>14 we'll give them to you.</p> <p>15 THE WITNESS: So just as an example, if</p> <p>16 we look at Jordan 2007, which has an odds ratio of</p> <p>17 1.00 --</p> <p>18 BY MS. PARFITT:</p> <p>19 Q Mm-hmm.</p> <p>20 A -- you find that one that would be</p> <p>21 interesting for me to circle.</p> <p>22 Q If it has a 1.0, I'd like you to circle</p> <p>23 it.</p> <p>24 A Sure.</p> <p>25 So in terms of your -- like, it's going</p>	<p style="text-align: right;">Page 349</p> <p>1 MS. PARFITT: Sure.</p> <p>2 BY MS. PARFITT:</p> <p>3 Q You have -- and maybe I can shorten this</p> <p>4 for you, how about that, in the interest of time.</p> <p>5 A Your call.</p> <p>6 Q We have -- thank you. I appreciate</p> <p>7 that.</p> <p>8 We've got about 32 studies here. How</p> <p>9 many of those studies reflect an odds ratio</p> <p>10 greater than 1.0?</p> <p>11 MS. BROWN: For a relative risk?</p> <p>12 MS. PARFITT: Correct.</p> <p>13 THE WITNESS: I don't know what to do</p> <p>14 with Moorman, because it's one study, right. Two</p> <p>15 different odds ratios.</p> <p>16 BY MS. PARFITT:</p> <p>17 Q Mm-hmm.</p> <p>18 A But it looks like above the dotted line,</p> <p>19 it's -- there's 24 studies, I guess, and then down</p> <p>20 below it, there's -- one, two, three, four,</p> <p>21 five -- there's 5 that are above 1.0, and you said</p> <p>22 above 1.0 this time, before you said --</p> <p>23 Q Above -- I did, above 1.0.</p> <p>24 A Because the including an odds ratio of</p> <p>25 1.00 is evidence of something above 1.0 would</p>

Gregory B. Diette, M.D.

Page 350	Page 352
<p>1 be --</p> <p>2 Q Right. So we're doing above 1.0.</p> <p>3 A Okay.</p> <p>4 Q You pointed that out, and you're right.</p> <p>5 A Yeah. So have I done it? There's one,</p> <p>6 two, three, four -- well, I guess Hartge is --</p> <p>7 one, two, three, four, five --</p> <p>8 Q Sure.</p> <p>9 A -- there's five down below the dotted</p> <p>10 line, and there were --</p> <p>11 Q Okay. And if you can just identify</p> <p>12 those where the point estimate does not exceed --</p> <p>13 it's not above 1.0.</p> <p>14 MS. BROWN: Counsel, can you represent,</p> <p>15 on the record, what this second up from the bottom</p> <p>16 is?</p> <p>17 MS. PARFITT: Sure. Hartge and Stewart,</p> <p>18 '94.</p> <p>19 MS. BROWN: Underneath that.</p> <p>20 MS. PARFITT: Wong.</p> <p>21 MS. BROWN: No, above -- what is the</p> <p>22 entry above Wong?</p> <p>23 MS. PARFITT: Oh, in his table --</p> <p>24 THE WITNESS: Oh, that too.</p> <p>25 MS. PARFITT: In his table he had RR</p>	<p>1 that those studies have a relative risk in excess</p> <p>2 of 1.0 demonstrate a positive result?</p> <p>3 MS. BROWN: Objection to the form.</p> <p>4 THE WITNESS: So some -- some of those,</p> <p>5 yes, and some of those, no.</p> <p>6 BY MS. PARFITT:</p> <p>7 Q All right. Would it be fair to say that</p> <p>8 they're certainly trending above the null; is that</p> <p>9 correct?</p> <p>10 MS. BROWN: Objection to the form.</p> <p>11 THE WITNESS: Not necessarily. I'm just</p> <p>12 trying to imagine like -- I think I understand why</p> <p>13 you're doing this -- but I'm just trying to</p> <p>14 imagine like standing in front of colleagues like</p> <p>15 with the Tzonou one and say, I've decided that a</p> <p>16 relative risk of 1.05 is a positive risk.</p> <p>17 I mean, you can only guess so close to</p> <p>18 1.0. I mean, 1.0 is basically null, right?</p> <p>19 There's no -- there's no effect. So you can hope</p> <p>20 for, but you're rarely going to get a 1.00. So if</p> <p>21 you get like a 1.01, 1.02, 1.03, those are</p> <p>22 basically 1.0.</p> <p>23 I mean, you can -- you can say -- try to</p> <p>24 make some point to somebody, Oh, it's a little bit</p> <p>25 above 1.0; therefore, it's a positive association.</p>
Page 351	Page 353
<p>1 0.03, RR 0.05. It was just extracted from his</p> <p>2 table.</p> <p>3 MS. BROWN: Oh, it's the second Hartge</p> <p>4 and Stewart.</p> <p>5 MS. PARFITT: Yeah.</p> <p>6 THE WITNESS: And so you want where just</p> <p>7 the midpoint is above the number 1.0?</p> <p>8 BY MS. PARFITT:</p> <p>9 Q Correct.</p> <p>10 A So Cramer, Harlow, Harlow, Chen, Cramer,</p> <p>11 Purdie, Chang, Cook, Green, Godard, Cramer, Ness,</p> <p>12 Mills, Cramer, Gates, Merritt; the two odds ratios</p> <p>13 for Moorman, Wu, Rosenblatt, Kurta, Kotsopoulos,</p> <p>14 Wu, Cramer, Schildkraut; and then one of the two</p> <p>15 Hartge's, Whittemore --</p> <p>16 Q And are you circling those, Doctor?</p> <p>17 A I'm not, no.</p> <p>18 Q Okay. If you could do that because</p> <p>19 we'll attach it as an exhibit. Sorry.</p> <p>20 A Should I just finish saying them --</p> <p>21 Q Sure.</p> <p>22 A -- and then go back and do it?</p> <p>23 So Rosenblatt, Tzonou, and that's it.</p> <p>24 So -- (circling studies.) Okay.</p> <p>25 Q Okay. What does the -- does the fact</p>	<p>1 But other than this setting, you're going to get</p> <p>2 laughed out of the room. I mean, this is -- this</p> <p>3 is a 1.05. So, you know, that's -- you call it</p> <p>4 what you want. I don't call that a positive</p> <p>5 finding.</p> <p>6 BY MS. PARFITT:</p> <p>7 Q Okay. Now, what I'd like you to do is</p> <p>8 look at the confidence intervals for each one of</p> <p>9 those studies, and circle where the confidence</p> <p>10 interval shows a relative risk of 1.2.</p> <p>11 MS. BROWN: Objection to the form of the</p> <p>12 question.</p> <p>13 BY MS. PARFITT:</p> <p>14 Q And again, if you will just circle</p> <p>15 those.</p> <p>16 A I -- I think you'd be better off drawing</p> <p>17 a line, right. Because it -- I mean, this scale</p> <p>18 here isn't really -- like there's no vertical</p> <p>19 scale that's labeled here. Right. So you've got</p> <p>20 1.0, 1.1 and 1.2. I mean if you want, I think you</p> <p>21 ought to just take a ruler and run it up from 1.2.</p> <p>22 Q Why don't you just go ahead and identify</p> <p>23 them, if you will, and we can go ahead and do</p> <p>24 that. Let's see.</p> <p>25 A Well, like I can --</p>

Gregory B. Diette, M.D.

Page 354	Page 356
<p>1 Q My question is just simply this: Would</p> <p>2 you identify all studies where the confidence</p> <p>3 interval is 1.2 or higher?</p> <p>4 MS. BROWN: Objection to the form.</p> <p>5 BY MS. PARFITT:</p> <p>6 Q And you can just circle them.</p> <p>7 A And it doesn't have to mean anything to</p> <p>8 me, right?</p> <p>9 Q Nope. Just circle anything where the</p> <p>10 confidence interval is above a 1.2.</p> <p>11 A So where the confidence interval</p> <p>12 includes 1.2?</p> <p>13 Q 1.2, correct.</p> <p>14 A Or where it's above 1.2?</p> <p>15 Q It's above 1.2.</p> <p>16 MS. BROWN: The entire interval?</p> <p>17 THE WITNESS: Well, so there's not many,</p> <p>18 right? So there's one --</p> <p>19 BY MS. PARFITT:</p> <p>20 Q You understand that it includes 1.2?</p> <p>21 A I heard -- oh, that's different,</p> <p>22 because there's only one where it's above 1.2.</p> <p>23 Q It includes the 1.2.</p> <p>24 A Or two that are above it.</p> <p>25 So the two that are above it, don't</p>	<p>1 was inconsistent.</p> <p>2 Q And that aspect --</p> <p>3 MS. BROWN: Are you looking at the</p> <p>4 report?</p> <p>5 THE WITNESS: Yeah.</p> <p>6 BY MS. PARFITT:</p> <p>7 Q -- was with regard to population study</p> <p>8 versus hospital-based studies?</p> <p>9 A Well, I think I made a comment about</p> <p>10 both, right?</p> <p>11 Q And if I can summarize your testimony,</p> <p>12 but feel free to look, but your testimony from the</p> <p>13 report -- or your writings and your report suggest</p> <p>14 that the case-control studies are inconsistent,</p> <p>15 and you focus on the fact that the hospital-based</p> <p>16 controls were inconsistent with the population-</p> <p>17 based controls.</p> <p>18 A That's one -- one of the areas of</p> <p>19 inconsistency.</p> <p>20 Q Okay. And you base that opinion on the</p> <p>21 fact that there -- the hospital-based studies were</p> <p>22 not statistically significant, but the</p> <p>23 population-based studies were statistically</p> <p>24 significant; is that correct?</p> <p>25 MS. BROWN: Objection to the form.</p>
Page 355	Page 357
<p>1 include it, right, so we got to start over.</p> <p>2 Q Everywhere -- sure. You go ahead and do</p> <p>3 it. Everywhere where the confidence interval is</p> <p>4 above -- includes 1.2.</p> <p>5 A That's all right. I'm just going to put</p> <p>6 a little asterisk next to them, because I already</p> <p>7 made a mark --</p> <p>8 Q Sure, that's fine.</p> <p>9 A -- next to the ones that are above 1.2.</p> <p>10 Okay.</p> <p>11 Q Okay. Let's go ahead and just put this</p> <p>12 here. I appreciate that.</p> <p>13 Okay. Here we go. Let's see here.</p> <p>14 Okay. So let's just stay with that one</p> <p>15 here for a moment. Let me give you -- give you a</p> <p>16 blank one here for a moment. Is that all right?</p> <p>17 So you have something in front of you.</p> <p>18 A Sure.</p> <p>19 Q Okay. All right.</p> <p>20 Dr. Diette, looking at the chart that we</p> <p>21 just talked about, you have described in your</p> <p>22 report that the case-control studies are</p> <p>23 inconsistent. Is that your testimony?</p> <p>24 A I think we should look literally at what</p> <p>25 I wrote, because I talked about one aspect that</p>	<p>1 THE WITNESS: That's one piece of</p> <p>2 evidence, right. So one piece of evidence is that</p> <p>3 the hospital-based ones, none of them were</p> <p>4 statistically significant, and some of the</p> <p>5 population-based ones were.</p> <p>6 BY MS. PARFITT:</p> <p>7 Q All right. And because you had some of</p> <p>8 the population-based studies, you found</p> <p>9 inconsistent because the confidence intervals were</p> <p>10 not -- were such that they were not statistically</p> <p>11 significant; is that correct?</p> <p>12 A That's a --</p> <p>13 MS. BROWN: Objection to the form.</p> <p>14 THE WITNESS: And as before, that's a</p> <p>15 piece of -- a piece of the information here.</p> <p>16 BY MS. PARFITT:</p> <p>17 Q Okay. I've reviewed your report. Other</p> <p>18 than the distinction between the statistical</p> <p>19 significance of studies versus the nonstatistical</p> <p>20 significance of studies, how else did you discern</p> <p>21 that they were different and not consistent?</p> <p>22 A Well, I have a section on consistency.</p> <p>23 So it -- there's other things about these studies</p> <p>24 that are inconsistent.</p> <p>25 So, for example, the -- the</p>

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 358</p> <p>1 dose-response relationships are all over the</p> <p>2 place. So that I found to be an inconsistency.</p> <p>3 The findings about certain kinds of ovarian</p> <p>4 cancers, some showed a particular cell type and</p> <p>5 some -- some didn't.</p> <p>6 Let me just --</p> <p>7 Q Let me ask you --</p> <p>8 MS. BROWN: Wait, I don't think he's</p> <p>9 finished.</p> <p>10 MS. PARFITT: No. Let's just make sure.</p> <p>11 THE WITNESS: I think we've said it, but</p> <p>12 I want to make it clear, right, because we were --</p> <p>13 we were really just sort of focused very -- very</p> <p>14 much on population-based and hospital-based case</p> <p>15 controls.</p> <p>16 BY MS. PARFITT:</p> <p>17 Q That's right.</p> <p>18 A But I think the fact that there is</p> <p>19 basically, you know, not a signal from the cohort</p> <p>20 studies is an inconsistency with studies of</p> <p>21 another design, so another form of inconsistency.</p> <p>22 I think that -- and what I've tried to</p> <p>23 say here, right, because I think -- I think some</p> <p>24 of these Hill criteria, it's hard to -- hard to</p> <p>25 keep every -- every comment you want under one</p>	<p style="text-align: right;">Page 360</p> <p>1 like that. So I'm -- that's more inconsistency.</p> <p>2 Q Okay. Dr. Diette, what I'm trying to</p> <p>3 get at here is, the underbelly, I guess, of your</p> <p>4 opinions seem to be from your report that cohort</p> <p>5 studies are inconsistent with the case-control</p> <p>6 studies, which they themselves are inconsistent</p> <p>7 because population-based studies and</p> <p>8 hospital-based studies, some were statistically</p> <p>9 significant and some were not. Correct?</p> <p>10 A Exactly, yes.</p> <p>11 Q Okay. And that's really the -- the guts</p> <p>12 of your report, correct?</p> <p>13 MS. BROWN: Objection to the form.</p> <p>14 THE WITNESS: I -- no. I mean, those</p> <p>15 are two very important points, but I'd say there's</p> <p>16 a heck of a lot more than that in the report.</p> <p>17 BY MS. PARFITT:</p> <p>18 Q Okay. Did you go through -- let's --</p> <p>19 let's talk a little bit about that.</p> <p>20 You described these relative risks of</p> <p>21 the case-control studies as small, weak -- small</p> <p>22 and weak, correct?</p> <p>23 A Correct.</p> <p>24 Q Okay. What type of -- those words</p> <p>25 "small and weak," are those scientific words?</p>
<p style="text-align: right;">Page 359</p> <p>1 particular heading, and so I've tried to get at</p> <p>2 this issue here too that if it were consistent</p> <p>3 that talc caused or was associated with ovarian</p> <p>4 cancer, I would expect to see it under a variety</p> <p>5 of circumstances, not just perineal dusting. And</p> <p>6 so one of the inconsistencies is that, you know,</p> <p>7 diaphragms and condoms, that we don't see that</p> <p>8 signal. So I'm just saying that that's an</p> <p>9 inconsistency. It's the opposite of consistency.</p> <p>10 And I guess too -- I mean just while</p> <p>11 we're even still on the -- on the types of</p> <p>12 studies, I mean the Taher study that, I guess, you</p> <p>13 know, even though it's not published yet, I mean</p> <p>14 they've got a summary risk for the hospital-based</p> <p>15 studies which is less than 1.0. Right. So now</p> <p>16 it's not even just like -- if -- I don't know</p> <p>17 whether we should like the Taher study or not, but</p> <p>18 it's out there, right. And so now we've got --</p> <p>19 Q It's out there. It's a piece of the</p> <p>20 evidence.</p> <p>21 A Yeah, it's something that's out there,</p> <p>22 so now we've got something that's unpublished from</p> <p>23 2018 that's got not even a positive risk. I mean,</p> <p>24 this -- this exercise of going to look and see</p> <p>25 what's over 1.0, there's a 0.94 or 6 or something</p>	<p style="text-align: right;">Page 361</p> <p>1 A So they're words that my colleagues and</p> <p>2 I use. I mean, it's a word that Dr. Rothman used</p> <p>3 when he did his analysis in 2000 and called the</p> <p>4 summary odds ratio or the risk -- risk of 1.3, he</p> <p>5 called it weak. I'm not sure whether he's citing</p> <p>6 a particular definition, but, you know, it --</p> <p>7 it's -- there's probably reasons, just like where</p> <p>8 you talk about a p-value of 0.05 not being the</p> <p>9 absolute line. I think it's why people have</p> <p>10 resisted trying to say that it has to be above an</p> <p>11 exact specific number.</p> <p>12 But I think we can all recognize risks</p> <p>13 that are large. You know, we know that a risk of</p> <p>14 10 is a large risk. We know that 20 is a large</p> <p>15 risk. We know that a relative risk of 1.01, it's</p> <p>16 got to be tiny, right, because it can't be any</p> <p>17 smaller than that on that particular scale.</p> <p>18 So somewhere in there we have to use</p> <p>19 some judgment, and I think if you got a 1.2 or</p> <p>20 1.3, I don't know who -- I don't know who thinks</p> <p>21 that's strong. It doesn't make any sense.</p> <p>22 Q Do you agree that having a weak</p> <p>23 association does not rule out a causal connection?</p> <p>24 MS. BROWN: Objection to the form.</p> <p>25 THE WITNESS: Wait a minute, say it</p>

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 362</p> <p>1 again because I think --</p> <p>2 BY MS. PARFITT:</p> <p>3 Q Having a weak association would not rule</p> <p>4 out a causal association.</p> <p>5 A That's correct.</p> <p>6 Q All right. Would you also agree that</p> <p>7 while the strength of an association is a</p> <p>8 guideline for drawing an inference of causation,</p> <p>9 there is no specified threshold required?</p> <p>10 MS. BROWN: Objection to the form.</p> <p>11 THE WITNESS: I don't think there's a</p> <p>12 specified threshold. I think it's a gradient,</p> <p>13 right, that you have to use as you're applying</p> <p>14 your judgment about all of the evidence. And that</p> <p>15 when you have a very small risk, you should be</p> <p>16 more concerned about the distorting effects of</p> <p>17 other factors, and if you have a larger risk, you</p> <p>18 can be less worried about those distorting</p> <p>19 factors.</p> <p>20 BY MS. PARFITT:</p> <p>21 Q But you will agree with me under the</p> <p>22 Bradford Hill factors, strong association or weak</p> <p>23 association, neither are necessary for finding</p> <p>24 causality, correct?</p> <p>25 MS. BROWN: Objection to the form.</p>	<p style="text-align: right;">Page 364</p> <p>1 Q Secondhand smoke and lung cancer.</p> <p>2 MR. LOCKE: Objection.</p> <p>3 THE WITNESS: I think really the Surgeon</p> <p>4 General has put it at -- it's either about 1.7 or</p> <p>5 1.9, somewhere in there.</p> <p>6 BY MS. PARFITT:</p> <p>7 Q Okay. Let me show you -- I'm sorry.</p> <p>8 1.7 or 1.9.</p> <p>9 Let me show you a study by Kim. And</p> <p>10 it's entitled "Exposure to Secondhand Smoke and</p> <p>11 the Risk of Cancer in Never Smokers." And I'll</p> <p>12 represent that it's in the International Journal</p> <p>13 of Environment, 2018. And this would be a</p> <p>14 meta-analysis by Dr. Kim.</p> <p>15 A Do you know, is it something I cited or</p> <p>16 is this new -- new to me or --</p> <p>17 Q I did not see it in your --</p> <p>18 A Okay. Thank you.</p> <p>19 Q -- list of references.</p> <p>20 In fact, good question. None of the 167</p> <p>21 articles that were in your curriculum vitae did I</p> <p>22 see that you cited in support for your expert</p> <p>23 report; is that correct?</p> <p>24 A That would -- I'm sure that's correct.</p> <p>25 Q Okay. Okay. Do you see that?</p>
<p style="text-align: right;">Page 363</p> <p>1 THE WITNESS: So there isn't a single</p> <p>2 one of his considerations that all by itself is</p> <p>3 completely necessary, right. It's a -- it's a</p> <p>4 method to pull together a variety of, you know,</p> <p>5 information about the studies. But he -- he</p> <p>6 certainly does give us some guidance about what</p> <p>7 "strong" and "not strong" might mean and the</p> <p>8 implications of that.</p> <p>9 BY MS. PARFITT:</p> <p>10 Q But we can agree sitting here today that</p> <p>11 those general terms, "weak," "small," do not</p> <p>12 dictate whether or not there is causality.</p> <p>13 MS. BROWN: Objection to the form.</p> <p>14 THE WITNESS: They don't dictate it.</p> <p>15 They inform it.</p> <p>16 BY MS. PARFITT:</p> <p>17 Q You mentioned that the -- I want to come</p> <p>18 back to that one in a second.</p> <p>19 Now, you, yourself, have actually done</p> <p>20 secondhand smoke studies, correct?</p> <p>21 A I've done studies that include</p> <p>22 secondhand smoke as a measure.</p> <p>23 Q Okay. What is your understanding of the</p> <p>24 relative risks for secondhand smoke?</p> <p>25 A For what?</p>	<p style="text-align: right;">Page 365</p> <p>1 A I do, yes.</p> <p>2 Q Okay. And if you look in the abstract,</p> <p>3 do you see where the authors determined that the</p> <p>4 relative risks for passive smoke exposure and lung</p> <p>5 cancer in never users was a relative risk rather</p> <p>6 than of 1.2.</p> <p>7 Do you see that? Take a moment.</p> <p>8 A Yeah.</p> <p>9 Q We'll put it on the ELMO.</p> <p>10 A So we're looking at the abstract?</p> <p>11 Q We are, mm-hmm.</p> <p>12 A And saying -- so odds ratio involving</p> <p>13 never smokers with significant exposure to</p> <p>14 secondhand compared to never smokers was 1.163.</p> <p>15 Q Okay. Do you see where it says:</p> <p>16 "Passive smoke exposure and lung cancer in never</p> <p>17 users was a relative risk of 1.245"?</p> <p>18 And we can go ahead and circle that.</p> <p>19 A That's for females?</p> <p>20 Q Yes.</p> <p>21 A For females, yeah, 1.245.</p> <p>22 Q Okay. So we had a 1.245 for females,</p> <p>23 and, I'm sorry, you said a 1.16 for secondhand all</p> <p>24 comers, right?</p> <p>25 A Exactly right.</p>

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 366</p> <p>1 Q Okay. Let me show you as well the Lv</p> <p>2 study, and it was a 2015 study. "Risk of</p> <p>3 All-Cause Mortality Associated With Secondhand</p> <p>4 Smoke."</p> <p>5 A Do I have that?</p> <p>6 Q I'm getting that for you. Hold on one</p> <p>7 second.</p> <p>8 A Oh, I'm sorry. I thought I --</p> <p>9 Q No, no worries.</p> <p>10 A I thought I missed it.</p> <p>11 (Diette Exhibit No. 23 was marked</p> <p>12 for identification.)</p> <p>13 BY MS. PARFITT:</p> <p>14 Q Do you have that in front of you?</p> <p>15 A Yes. So this is by Lv?</p> <p>16 Q That's right.</p> <p>17 A The last name, yeah.</p> <p>18 Q And now again, looking at the abstract</p> <p>19 section, does it report the relative risk for</p> <p>20 never smokers exposed to secondhand smoke versus</p> <p>21 unexposed?</p> <p>22 A So the pooled relative risk for never</p> <p>23 smokers compared to those -- is that -- so that</p> <p>24 first sentence of the results --</p> <p>25 Q That's right --</p>	<p style="text-align: right;">Page 368</p> <p>1 associations that are implementing those types of</p> <p>2 programs to reduce secondhand smoke for fear of</p> <p>3 lung cancer have accepted this type of data, 1.1,</p> <p>4 1.2, for purposes of making those policy</p> <p>5 decisions?</p> <p>6 A So I don't know --</p> <p>7 MR. LOCKE: Objection.</p> <p>8 THE WITNESS: Oops, sorry.</p> <p>9 Like, I don't -- I don't know what</p> <p>10 inputs they -- they used, and I don't -- I'm not</p> <p>11 saying they wouldn't, but I don't know whether</p> <p>12 they would use these risks to drive that or not.</p> <p>13 BY MS. PARFITT:</p> <p>14 Q Okay. You would agree with me, though,</p> <p>15 that the risk of 1.1 and 1.2 are very -- are</p> <p>16 actually less than the relative risks that we've</p> <p>17 seen with talcum powder products and ovarian</p> <p>18 cancer, correct?</p> <p>19 MS. BROWN: Objection to the form.</p> <p>20 THE WITNESS: So it's less than the</p> <p>21 pooled odds ratio from the case-control studies in</p> <p>22 the meta-analyses.</p> <p>23 BY MS. PARFITT:</p> <p>24 Q Okay. Now, you yourself have done</p> <p>25 studies on indoor particulate matter, correct?</p>
<p style="text-align: right;">Page 367</p> <p>1 A -- 1.18?</p> <p>2 Q Correct. And they then report in the</p> <p>3 all-cause mortality and RR was 1.23 for</p> <p>4 cardiovascular diseases. Do you see that?</p> <p>5 A Yeah, although -- exactly right, yep.</p> <p>6 Q Okay. Now, there have been -- and this</p> <p>7 is work that you do as well, correct?</p> <p>8 MS. BROWN: Objection to the form.</p> <p>9 BY MS. PARFITT:</p> <p>10 Q You do research work on secondhand</p> <p>11 smoke?</p> <p>12 A I have done, yeah, and still do.</p> <p>13 Q Okay. And are you aware that in the</p> <p>14 United States and in other countries, there have</p> <p>15 been health programs implemented to reduce</p> <p>16 secondhand smoke based upon relative risks, like</p> <p>17 you've just seen, 1.1, 0.8, 1.2?</p> <p>18 MR. LOCKE: Objection.</p> <p>19 THE WITNESS: I mean, I don't know if</p> <p>20 the programs were based on these studies, and</p> <p>21 there certainly have been higher relative risks</p> <p>22 before. But I -- but I agree that there are</p> <p>23 programs to reduce secondhand smoke exposure.</p> <p>24 BY MS. PARFITT:</p> <p>25 Q Okay. And would you agree today that</p>	<p style="text-align: right;">Page 369</p> <p>1 A Correct.</p> <p>2 Q Okay. In particular, you published a</p> <p>3 study with McCormack and Diette on common</p> <p>4 household exposures?</p> <p>5 A I've published a bunch with her, so I</p> <p>6 don't know which -- which particular one that is.</p> <p>7 Q All right. It's Common -- it's Common</p> <p>8 Household Products, 2008." McCormack is the lead</p> <p>9 article -- author.</p> <p>10 A What journal?</p> <p>11 Q It is in the Environmental Res,</p> <p>12 Environmental --</p> <p>13 A Environmental research.</p> <p>14 Q -- Research. And it's dated February</p> <p>15 2008. And take a minute to --</p> <p>16 (Diette Exhibit No. 24 was marked</p> <p>17 for identification.)</p> <p>18 BY MS. PARFITT:</p> <p>19 Q Do you have that in front of you?</p> <p>20 A I do.</p> <p>21 Q Okay. Now, if you look at the first</p> <p>22 page under the abstract, about the third line</p> <p>23 down -- excuse me, fourth line down, it says:</p> <p>24 "There is a public health imperative to</p> <p>25 characterize indoor source as being less</p>

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 370</p> <p>1 extensively characterized" -- excuse me. I'm</p> <p>2 sorry.</p> <p>3 "There is a public health imperative to</p> <p>4 characterize indoor sources of PM" -- I assume</p> <p>5 that's particulate matter?</p> <p>6 A Correct.</p> <p>7 Q -- "with this vulnerable population to</p> <p>8 enable effective intervention strategies."</p> <p>9 Did I read that correctly?</p> <p>10 A You did.</p> <p>11 Q Okay. You were the lead -- one of the</p> <p>12 lead authors in that study?</p> <p>13 A Yeah, I was, by position, the senior</p> <p>14 author, but I was the head of the -- the study</p> <p>15 that produced this paper.</p> <p>16 Q All right. And what is -- and do you</p> <p>17 have an opinion with regard to what the relative</p> <p>18 risks are for indoor ambient particulate matter?</p> <p>19 A For what?</p> <p>20 Q For --</p> <p>21 A You mean qualitative, like what</p> <p>22 illnesses they cause or --</p> <p>23 Q Yes, with regard -- I believe you</p> <p>24 studied a bit of asthma, so I believe it would be</p> <p>25 the relative risk of indoor particulates and</p>	<p style="text-align: right;">Page 372</p> <p>1 MS. BROWN: Objection to the form. You</p> <p>2 need the disease to link the --</p> <p>3 MS. PARFITT: Lung. Lung.</p> <p>4 MS. BROWN: You mean cancer? Objection</p> <p>5 to the form.</p> <p>6 THE WITNESS: Anyway, I can't answer it.</p> <p>7 You need more in the sentence or the question in</p> <p>8 order for me to be able to answer it.</p> <p>9 BY MS. PARFITT:</p> <p>10 Q Okay. Are there any -- fair enough.</p> <p>11 Are there any reported relative risks</p> <p>12 between indoor particulate matter and lung</p> <p>13 disease?</p> <p>14 MS. BROWN: Objection to the form.</p> <p>15 THE WITNESS: I'd want to be super</p> <p>16 careful about what we're saying is lung disease,</p> <p>17 because some people might think that that means</p> <p>18 the risk of developing a particular lung disease,</p> <p>19 and others might mean the worsening of an existing</p> <p>20 disease or a lung function abnormality.</p> <p>21 BY MS. PARFITT:</p> <p>22 Q Okay. Do you know what the relative</p> <p>23 risk is between indoor particulate matter and</p> <p>24 asthma?</p> <p>25 A The risk of developing asthma?</p>
<p style="text-align: right;">Page 371</p> <p>1 asthma?</p> <p>2 A Well, there's not one single way to</p> <p>3 answer that, right. So this -- this paper doesn't</p> <p>4 look like the one that's actually quantified it,</p> <p>5 right. We have other ones that look at the</p> <p>6 increase in, say, symptoms, for example, or</p> <p>7 exacerbations per very small increment in</p> <p>8 particulate matter.</p> <p>9 So like, I think if you -- if you're</p> <p>10 looking at our studies, you're not going to find a</p> <p>11 relative risk that's, like -- that's analogous to</p> <p>12 these where this is the relative risk of an</p> <p>13 outcome for secondhand smoke, yes/no. Ours are</p> <p>14 reported not by that but by little tiny increments</p> <p>15 or decrements of -- of particle concentrations.</p> <p>16 Q Do you know what the relative risk is</p> <p>17 for indoor ambient air?</p> <p>18 A That's --</p> <p>19 MS. BROWN: Objection to the form.</p> <p>20 THE WITNESS: That's not a full</p> <p>21 question.</p> <p>22 BY MS. PARFITT:</p> <p>23 Q Do you -- is there a relative risk for</p> <p>24 exposure to the lungs in indoor particulate</p> <p>25 matter?</p>	<p style="text-align: right;">Page 373</p> <p>1 Q Correct.</p> <p>2 A It's not --</p> <p>3 MS. BROWN: Objection to the form.</p> <p>4 THE WITNESS: Sorry. It's not known.</p> <p>5 BY MS. PARFITT:</p> <p>6 Q It's not known.</p> <p>7 A Not known.</p> <p>8 Q It's not been published.</p> <p>9 A Well, I can't say there's not a single</p> <p>10 paper out there, but at this point the -- a</p> <p>11 summary of the evidence is that we can't say for</p> <p>12 sure that it's -- that it causes asthma.</p> <p>13 Q Have you reviewed in any of the</p> <p>14 literature published data with regard to airborne</p> <p>15 particles -- indoor airborne particles and asthma</p> <p>16 as to what the relative risk may be?</p> <p>17 MS. BROWN: Objection to form.</p> <p>18 THE WITNESS: Relative risk of?</p> <p>19 BY MS. PARFITT:</p> <p>20 Q Relative risk of asthma from exposure to</p> <p>21 indoor air particulate.</p> <p>22 MS. BROWN: Objection to the form.</p> <p>23 THE WITNESS: So I -- I've read a ton of</p> <p>24 stuff about it. I mean if you've got a particular</p> <p>25 article, I'm happy to read it and interpret it.</p>

Gregory B. Diette, M.D.

Page 374	Page 376
<p>1 But as of this point, I think we -- should I</p> <p>2 explain or just --</p> <p>3 BY MS. PARFITT:</p> <p>4 Q No, I -- all I really want to know in</p> <p>5 the interest of time is whether or not you have</p> <p>6 reviewed any of the scientific literature data</p> <p>7 that reports what the relative risk is for indoor</p> <p>8 particulate matter and the risk of getting asthma?</p> <p>9 MS. BROWN: Objection to the form.</p> <p>10 BY MS. PARFITT:</p> <p>11 Q And if you haven't, that's fine.</p> <p>12 A Oh, my gosh, no, it's not that. I have.</p> <p>13 I just don't think that you can answer that</p> <p>14 question. I'm not saying there's not some study</p> <p>15 out there that may estimate a risk for that, but</p> <p>16 it isn't established. Like, at this point, we</p> <p>17 cannot say in 2019 that indoor particulate matter</p> <p>18 causes asthma.</p> <p>19 And -- and you have to say more to the</p> <p>20 sentence. So let's just talk about like adults</p> <p>21 living in the city. We can't say that. You</p> <p>22 know -- you know, there's -- there's studies that</p> <p>23 have looked at the relative risk of indoor</p> <p>24 cooking, which is predominantly particulate</p> <p>25 matter, in developing countries, but even the</p>	<p>1 meter cubed. It may be from a particular source,</p> <p>2 like traffic-related pollution or not.</p> <p>3 I mean there's more to it. There's not</p> <p>4 just like some summary that -- that I can -- I can</p> <p>5 make. Maybe you can find somebody that can just</p> <p>6 say particulate matter has this risk of causing</p> <p>7 asthma. I haven't seen it.</p> <p>8 But it's not there aren't like a whole</p> <p>9 bunch of studies looking at the relationship</p> <p>10 between indoor and outdoor particulate matter and</p> <p>11 lung disease as both, you know, developing newly</p> <p>12 and worsening the existing ones.</p> <p>13 BY MS. PARFITT:</p> <p>14 Q Right. Does secondhand smoke cause lung</p> <p>15 cancer?</p> <p>16 MS. BROWN: Objection to the form.</p> <p>17 THE WITNESS: It seems -- it seems that</p> <p>18 that -- that has been established.</p> <p>19 (Counsel conferring.)</p> <p>20 BY MS. PARFITT:</p> <p>21 Q Okay. Let's talk a little bit --</p> <p>22 THE WITNESS: We're just doing a time</p> <p>23 check. I'm just trying -- do you know roughly how</p> <p>24 much we --</p> <p>25 THE VIDEOGRAPHER: Five hours, 34</p>
Page 375	Page 377
<p>1 asthma evidence is not fully developed.</p> <p>2 So it's just -- it's one of those things</p> <p>3 where you may find a paper that has an estimate,</p> <p>4 but it hasn't been fully established yet.</p> <p>5 Q All right. Do you -- I understand it's</p> <p>6 not fully established, but are there reported</p> <p>7 relative risks from the scientific literature?</p> <p>8 MS. BROWN: Objection.</p> <p>9 THE WITNESS: I'm sure there are.</p> <p>10 MS. BROWN: Objection --</p> <p>11 THE WITNESS: I'm sure there are, but --</p> <p>12 BY MS. PARFITT:</p> <p>13 Q There are. Do you know what they are?</p> <p>14 MS. BROWN: Objection to the form.</p> <p>15 THE WITNESS: Oh, my gosh.</p> <p>16 BY MS. PARFITT:</p> <p>17 Q If you know. If -- like, do you know</p> <p>18 there is a range of relative risks between</p> <p>19 exposure to indoor particulate matter and asthma?</p> <p>20 MS. BROWN: Objection to the form of the</p> <p>21 question.</p> <p>22 THE WITNESS: I've got to see what</p> <p>23 you're talking about, because I think that when</p> <p>24 you ask it that way, there may be some estimate</p> <p>25 based on a particular number of micrograms per</p>	<p>1 minutes.</p> <p>2 THE WITNESS: So a little under an hour</p> <p>3 and a half? Did you guys want to do a --</p> <p>4 MS. PARFITT: A quick break here? Sure.</p> <p>5 THE WITNESS: -- or a break here or</p> <p>6 wait?</p> <p>7 MS. PARFITT: No, that's fine. We can</p> <p>8 take a quick one now. That's fine.</p> <p>9 THE VIDEOGRAPHER: The time is 3:50 p.m.</p> <p>10 We're going off the record.</p> <p>11 (Recess.)</p> <p>12 THE VIDEOGRAPHER: The time is 4:10 p.m.</p> <p>13 We're back on the record.</p> <p>14 We're on the record, by the way.</p> <p>15 (A discussion was held off the record.)</p> <p>16 (Diette Exhibit Nos. 25 and 26</p> <p>17 were marked for identification.)</p> <p>18 BY MS. PARFITT:</p> <p>19 Q Are you ready, Dr. Diette?</p> <p>20 A I am. Thank you.</p> <p>21 Q Very good.</p> <p>22 THE VIDEOGRAPHER: Microphone, Counsel.</p> <p>23 BY MS. PARFITT:</p> <p>24 Q Dr. Diette, I -- I asked you a little</p> <p>25 bit earlier about the relative risk for secondhand</p>

95 (Pages 374 to 377)

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 378</p> <p>1 smoke and -- and lung cancer. 2 And what I would like you to do is -- 3 and I apologize, I don't have copies of this -- so 4 I'm showing you what is the report of the Surgeon 5 General, I believe it was back in 2006, "The 6 Health Consequences of Involuntary Exposure to 7 Tobacco Smoke, A Report of the Surgeon General." 8 Have you read that in the past? 9 A So definitely not every word, but I've 10 read big chunks of it. 11 Q Okay. I figured with your work you may 12 have. 13 A Yeah. 14 Q All right. Let me direct your attention 15 to -- 16 MS. PARFITT: And I apologize to all, so 17 you have to look on the camera -- on the screen. 18 MS. BROWN: Okay. So just for the 19 record, we don't have copies of this, and so I 20 will object to the fact that we have no context or 21 ability to look at the document ourselves. 22 MS. PARFITT: All right. 23 BY MS. PARFITT: 24 Q And again, Doctor, you've reviewed this 25 report, correct, in the past?</p>	<p style="text-align: right;">Page 380</p> <p>1 Q That's all right. 2 -- is related to secondhand smoke and 3 lung cancer? 4 MS. BROWN: Objection to the form. 5 THE WITNESS: It looks like it there. I 6 remember there's other numbers in there as well, 7 but I mean, I remember it being 1-point something 8 and -- 9 BY MS. PARFITT: 10 Q Does that refresh my memory? 11 MS. BROWN: Well, let him finish, 12 please. 13 THE WITNESS: I think there's somewhere 14 else in there where there's other estimates, but 15 still not like -- not sky high. Still less than 16 2.0. 17 BY MS. PARFITT: 18 Q But you don't disagree with the Surgeon 19 General's conclusion that the pooled evidence 20 indicates a 20 to 30 percent increase in the risk 21 of lung cancer from secondhand smoke exposure 22 associated with living with a smoker, correct? 23 MR. LOCKE: Objection. 24 MS. BROWN: Objection. He doesn't have 25 the document, he can't review it.</p>
<p style="text-align: right;">Page 379</p> <p>1 A In the past, and I've read parts of it, 2 but as you know, I mean it's a humongous -- 3 Q It is big. 4 A -- document, and so some parts 5 weren't -- weren't for me. 6 Q All right. I want to focus your 7 attention on the conclusions of the Surgeon 8 General's report. 9 And 1: "The evidence is sufficient to 10 infer a causal relationship between secondhand 11 smoke exposure and lung cancer among lifetime 12 nonsmokers. This conclusion extends to all 13 secondhand smoke exposure, regardless of location. 14 "2. The pooled evidence that indicates" 15 -- sorry -- "the pooled evidence indicates a 20 to 16 30 percent" -- that would be a 1.2 or 1.3 relative 17 risk -- "increase in the risk of lung cancer from 18 secondhand smoke exposure associated with a 19 smoker." 20 Did I read that correctly? 21 A You did. 22 Q And is that what the -- are those the 23 numbers, 1.2 and 1.3, the relative risks that the 24 Surgeon General has concluded is -- 25 A Um -- I'm sorry.</p>	<p style="text-align: right;">Page 381</p> <p>1 BY MS. PARFITT: 2 Q Are you disputing that conclusion? 3 MS. BROWN: Objection. He has no basis 4 to do it, he doesn't have the document. 5 BY MS. PARFITT: 6 Q Are you disputing that, Doctor? 7 A I would -- 8 MR. LOCKE: Objection. 9 THE WITNESS: I would say it fits with 10 what I understood to be true at the time that that 11 was published. 12 BY MS. PARFITT: 13 Q Fair enough. Thank you. I appreciate 14 that. 15 Dr. Diette, is it fair that -- to say 16 that we don't have, and you've not reviewed, any 17 Johnson -- Johnson & Johnson specific epidemiology 18 with regard to a study of just Johnson & Johnson 19 Baby Powder? 20 MS. BROWN: Objection to the form. 21 THE WITNESS: That is correct. 22 BY MS. PARFITT: 23 Q Okay. And so what we rely on, and what 24 you've relied on, rather, is data and 25 epidemiological science on all comers, all brands,</p>

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 382</p> <p>1 correct?</p> <p>2 MS. BROWN: Objection to the form.</p> <p>3 MR. LOCKE: Objection.</p> <p>4 THE WITNESS: I -- I wouldn't</p> <p>5 characterize it exactly that way. I mean I would</p> <p>6 say that I can't really sort between different</p> <p>7 brands based on the epidemiologic literature, but</p> <p>8 whatever all brands is, I don't -- you know, I</p> <p>9 don't know what that represents.</p> <p>10 BY MS. PARFITT:</p> <p>11 Q And would it be fair then if one product</p> <p>12 that contained -- one product, talcum powder</p> <p>13 product contained asbestos, and another did not,</p> <p>14 that would result in a conclusion that would draw</p> <p>15 it towards the null? Is that fair?</p> <p>16 MS. BROWN: Objection to the question.</p> <p>17 THE WITNESS: I don't understand that.</p> <p>18 BY MS. PARFITT:</p> <p>19 Q Okay.</p> <p>20 A I mean I understand the idea of drawing</p> <p>21 something to the null. I just don't understand --</p> <p>22 Q Sure.</p> <p>23 A -- what preceded that.</p> <p>24 Q If you have a product like Johnson &</p> <p>25 Johnson, and you -- and it has a carcinogen in it,</p>	<p style="text-align: right;">Page 384</p> <p>1 BY MS. PARFITT:</p> <p>2 Q Okay. When you say it doesn't change</p> <p>3 the totality of the evidence that we have</p> <p>4 available for us, isn't it true that the presence</p> <p>5 of a carcinogen, like asbestos in talcum powder</p> <p>6 products, supports the biological -- biologically</p> <p>7 plausible mechanism for association between talcum</p> <p>8 powder products and ovarian cancer?</p> <p>9 MS. BROWN: Objection to the form of the</p> <p>10 question.</p> <p>11 THE WITNESS: I -- I'd say no. And for</p> <p>12 reasons, if you want them, or just leave it at no.</p> <p>13 BY MS. PARFITT:</p> <p>14 Q Well, you've testified that asbestos is</p> <p>15 a carcinogen. Correct?</p> <p>16 A Correct.</p> <p>17 Q All right. And the fact that asbestos</p> <p>18 might be in the talcum powder product does not</p> <p>19 impact your opinions with regard to the increased</p> <p>20 biologically plausible mechanism for talc to cause</p> <p>21 ovarian cancer.</p> <p>22 MS. BROWN: Objection to the form. Are</p> <p>23 you talking about a Johnson & Johnson product?</p> <p>24 MS. PARFITT: Just generally.</p> <p>25 MS. BROWN: Objection to the form.</p>
<p style="text-align: right;">Page 383</p> <p>1 and you lump it together with other products that</p> <p>2 are not infected or contaminated with asbestos,</p> <p>3 what does that do to the overall relative risk --</p> <p>4 A Oh.</p> <p>5 Q -- when studying that product?</p> <p>6 MS. BROWN: Objection to the incomplete</p> <p>7 hypothetical.</p> <p>8 THE WITNESS: So concept and reality,</p> <p>9 right. So the concept would be, if you knew that</p> <p>10 there were enough asbestos that led to an exposure</p> <p>11 that was enough in order to cause a disease from</p> <p>12 one product, and it was pooled with another</p> <p>13 product that didn't have that same amount or</p> <p>14 didn't have any asbestos but you knew that there</p> <p>15 was enough to cause disease, then it would -- it</p> <p>16 would do exactly what you're saying, is it would</p> <p>17 move it towards -- towards one.</p> <p>18 The reality is there wouldn't be any</p> <p>19 impact whatsoever because the epidemiology already</p> <p>20 takes into account whatever those brands are, and</p> <p>21 so it doesn't change the totality of the evidence</p> <p>22 that we have available for us.</p> <p>23 So concept, I mean you could sort of</p> <p>24 imagine what you're saying to be true, but</p> <p>25 reality, no.</p>	<p style="text-align: right;">Page 385</p> <p>1 THE WITNESS: It -- it does not.</p> <p>2 As you ask these things, I'm trying to</p> <p>3 figure out if I'm supposed to explain what I'm</p> <p>4 saying or is --</p> <p>5 MS. BROWN: No, you answered the</p> <p>6 question.</p> <p>7 THE WITNESS: Okay.</p> <p>8 MS. BROWN: She'll ask you another one</p> <p>9 if she has one.</p> <p>10 THE WITNESS: Okay. All right.</p> <p>11 BY MS. PARFITT:</p> <p>12 Q Does Johnson & Johnson sell baby powder</p> <p>13 that's 99 percent asbestos and 1 percent</p> <p>14 fragrance?</p> <p>15 MS. BROWN: Objection to the form of the</p> <p>16 question.</p> <p>17 THE WITNESS: If they do, I'm not aware</p> <p>18 of that.</p> <p>19 BY MS. PARFITT:</p> <p>20 Q Okay. And if I understand, the presence</p> <p>21 of asbestos in a talcum powder product does not in</p> <p>22 your mind impact the biologically plausible</p> <p>23 mechanism for talcum powder products to cause</p> <p>24 ovarian cancer.</p> <p>25 MR. LOCKE: Objection.</p>

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 386</p> <p>1 THE WITNESS: No, there's not enough 2 information in what you said there. 3 BY MS. PARFITT: 4 Q What would you need? 5 A So I would need a couple of things. One 6 is I would need to have some estimate of what the 7 dose would be, and some assurance from somewhere, 8 which I don't have, that that represented a dose 9 that was sufficient to cause -- and by dose, I'm 10 talking about dose of asbestos, right -- that that 11 was a sufficient dose to cause ovarian cancer. 12 And based on what I've seen, I can't 13 make that link. I can't -- I haven't seen 14 anything that says that there's a plausible 15 concentration or dose that people would be exposed 16 to that links to anything I can find in the 17 epidemiologic literature about how much, if any, 18 it would take in order to -- to cause ovarian 19 cancer. And what I -- should I finish? 20 Q Mm-hmm, yeah, finish. 21 A Okay. I'm sorry. 22 Q I'm trying not to interpret you. 23 A No, no, you're not. I didn't mean -- I 24 didn't think you were. 25 Q So doing better.</p>	<p style="text-align: right;">Page 388</p> <p>1 And then I think if you -- if you pair 2 that with more modern studies, if you take like 3 the Reid study from Australia, you take women who 4 worked, you know, in and around a crocidolite 5 mine, they certainly had enough exposure to get 6 asbestos-related diseases, but they don't get 7 ovarian cancer. 8 And so I think that the -- you know, the 9 sum total of all that just -- it doesn't make 10 sense that just knowing the fact that there's some 11 particle -- even if it's true, that some particle 12 of asbestos is going to be enough to cause 13 disease. 14 Q Okay. Have you -- have you read -- I 15 didn't see it in your reliance list -- Reid, 2012? 16 A I have two Reeds, I think, and if I only 17 listed one, I meant to include two. 18 Q Yeah, you only listed 2011 Reid. You 19 didn't list 2012 Reid. 20 A I meant -- so I don't know which one is 21 there. There's one from Whitnum, which is the 22 study of the women that -- you know, that I was 23 just describing, and a separate one is -- it's 24 basic -- basically like a meta-analysis or a 25 reanalysis of the ovarian cancer and asbestos</p>
<p style="text-align: right;">Page 387</p> <p>1 A I didn't think you were. 2 So I mean there's more, right. I mean 3 so the -- if you look at IARC and what those 4 studies represented, they represent for the most 5 part -- and by IARC, I'm talking about IARC and 6 ovarian cancer and asbestos -- you know, mostly 7 circumstances that aren't typical of American 8 women. For example, so women in Europe who were 9 working at a time and place when there was 10 different forms and lots of asbestos that may have 11 been sufficient to cause other asbestos-related 12 diseases. 13 So if you -- if those -- if those 14 findings are absolutely accurate -- you know, you 15 take away the issue of misclassification or 16 anything else -- if they're absolutely accurate, 17 you've got a relative risk in the neighborhood of 18 like 1.75 or something like that. 19 So I'm not saying that's not an 20 important risk, but it's not a huge risk, right? 21 So we're taking heavy industrial exposure to get 22 to a 1.75. I haven't seen anything that could 23 tell me that anything we're talking about here 24 could possibly rise to the level of heavy 25 industrial exposure.</p>	<p style="text-align: right;">Page 389</p> <p>1 literature. 2 Q Okay. Do you recall from your reading 3 that the scientists in Reid 2012 determined that 4 childhood exposure to asbestos was associated with 5 an increased risk of cancer mortality which was 6 3.5 times greater than the general population? Do 7 you recall those numbers? 8 A I don't, but cancer mortality to -- 9 MS. BROWN: Objection. 10 THE WITNESS: Can you tell me which -- 11 because I don't remember which year links to which 12 Reid study. 13 BY MS. PARFITT: 14 Q That was the 2012 that I was speaking 15 of. 16 A No, I understand that. I heard the 17 year, but I don't know what the title is. 18 Q Oh, the title is "All-cause mortality in 19 cancer incidence among adults exposed to blue 20 asbestos during childhood." 21 A I think that's a third study then, 22 because I think the two I'm referring to are -- 23 are two different ones. 24 Q All right. So did you read the 2012 or 25 that just wasn't one you read?</p>

Gregory B. Diette, M.D.

Page 390	Page 392
<p>1 MS. BROWN: Well, Counsel, can you show 2 it to him and he'll tell you? 3 MS. PARFITT: Sure. 4 THE WITNESS: I don't know if either of 5 the ones that I cite, you know, that I'm familiar 6 with are from 2012, but I don't think I read the 7 one that you're talking about. 8 BY MS. PARFITT: 9 Q Okay. From looking at your curriculum 10 vitae and the studies you cited, you cited Reid -- 11 actually you cited three Reids. You cited Reid 12 2011, you cited Reid 2008, and you cited Reid 13 2009. The study that you did not cite was Reid 14 2012. 15 A That -- that sounds believable. That 16 makes sense. 17 Q All right. So for purposes of the 18 opinions in your report, you did not rely on Reid 19 2012, is that fair? 20 MS. BROWN: Objection to the form of the 21 question. 22 THE WITNESS: I -- I don't think I'm 23 familiar with that study. 24 BY MS. PARFITT: 25 Q Okay. Fair enough.</p>	<p>1 THE WITNESS: I'm not disagreeing with 2 you, I think that's the language they use, but 3 they -- they used their -- their strongest -- 4 their strongest grading. 5 BY MS. PARFITT: 6 Q How many of the IARC studies that formed 7 the basis for IARC's conclusion that asbestos 8 causes ovarian cancer was there information 9 concerning the exposure and the dose? 10 A So I think you said something that you 11 didn't mean to, because I think you said how many 12 of the IARC studies that IARC considered. I 13 think -- did you mean how many of the underlying 14 studies that IARC considered? 15 Q Correct. 16 A Okay. And so there's at least five that 17 I remember that were like sort of factory worker 18 type studies, and then I think there were a couple 19 of more. I'd have to go back, though, to look and 20 see what -- what they had about dose, if anything. 21 My -- I'm thinking like at least for the World 22 War II era ones, they probably didn't have good 23 measures at all, you know, if any. 24 Q Okay. Let me show you what I will have 25 marked as Exhibit 27.</p>
Page 391	Page 393
<p>1 Are you able to share with us, 2 Dr. Diette, what the minimum dose of asbestos is 3 necessary in order to cause an ovarian cancer? 4 MS. BROWN: Objection to the form of the 5 question. 6 THE WITNESS: I haven't seen that 7 published. I can tell you that at least in one of 8 those Whitnum studies that women were exposed to 9 as much as 40 fiber/cc years cumulatively of 10 crocidolite, and -- and that apparently wasn't 11 enough to cause ovarian cancer. But I didn't see, 12 you know, good measurements or estimates from 13 the -- the more historic to say what the exposures 14 were. 15 BY MS. PARFITT: 16 Q Okay. IARC looked at the issue of 17 asbestos and ovarian cancer, correct? 18 A They did. 19 MS. BROWN: Form. 20 THE WITNESS: Sorry. 21 BY MS. PARFITT: 22 Q All right. IARC concluded that asbestos 23 causes ovarian cancer. 24 MS. BROWN: Form. 25 MR. LOCKE: Objection.</p>	<p>1 (Diette Exhibit No. 27 was marked 2 for identification.) 3 MR. ROSEN: 26, for the record, is the 4 Surgeon General's report, which we'll supplement 5 with a paper copy. 6 THE WITNESS: The same one -- the same 7 one that we were talking about before the 8 secondhand smoke or involuntary smoke? 9 MR. ROSEN: Right, so there won't be a 10 26 in the file. 11 THE WITNESS: Got you. 12 BY MS. PARFITT: 13 Q Let me show you what we have marked as 14 Exhibit 27. 15 Do you have that in front of you? 16 A I have the "Arsenic, Metals, Fibres and 17 Dusts," 100C IARC. 18 Q That's correct, that's the right one. 19 Okay. Let me direct your attention to 20 the bottom of page 253. 21 Do you have that? 22 A 253? 23 Q 253, correct. 24 A I do. 25 Q All right. And it says: "An</p>

99 (Pages 390 to 393)

Gregory B. Diette, M.D.

Page 394	Page 396
<p>1 examination of the association between asbestos</p> <p>2 and ovarian cancer was not undertaken by the IOM,"</p> <p>3 and then it has a 2000 -- a 2006 date. Correct?</p> <p>4 A Yes.</p> <p>5 Q Okay. Now, before we get to Table 2.8,</p> <p>6 what I want you to do is turn over to page 256.</p> <p>7 All right. And again, directing your</p> <p>8 attention to the far right column. Are you there?</p> <p>9 And it starts with, "Working group"?</p> <p>10 A I am. I'm sorry, I'm distracted because</p> <p>11 I think there's --</p> <p>12 MS. BROWN: It has a weird --</p> <p>13 THE WITNESS: -- there's like a font</p> <p>14 issue or something, like somebody's printer didn't</p> <p>15 have the right --</p> <p>16 BY MS. PARFITT:</p> <p>17 Q That might have been ours. I apologize.</p> <p>18 Not ideal circumstances.</p> <p>19 All right. Do you see where it says,</p> <p>20 "The working group"?</p> <p>21 A I do.</p> <p>22 Q All right. "The working group noted</p> <p>23 that a causal association between exposure to</p> <p>24 asbestos and cancer of the ovary was clearly</p> <p>25 established based on five strongly positive cohort</p>	<p>1 Q Okay. Do you see where the working</p> <p>2 group of IARC considered all of the data, and they</p> <p>3 made a determination that there were not, at the</p> <p>4 bottom, sufficient -- they ruled out the</p> <p>5 possibility that there may have been a</p> <p>6 misdiagnosis.</p> <p>7 Do you see that?</p> <p>8 MS. BROWN: Objection to the form.</p> <p>9 THE WITNESS: I see that they've -- that</p> <p>10 they reached that -- that conclusion.</p> <p>11 BY MS. PARFITT:</p> <p>12 Q Okay. And that's different than the</p> <p>13 conclusion you raised in your report, correct?</p> <p>14 A Well, it's different --</p> <p>15 MS. BROWN: Objection.</p> <p>16 THE WITNESS: It is different, yes.</p> <p>17 BY MS. PARFITT:</p> <p>18 Q All okay. Right. Let's go back to</p> <p>19 again page 253.</p> <p>20 And you will see it references a table,</p> <p>21 Table 2.8. Do you see that on the top of 254?</p> <p>22 A Okay.</p> <p>23 Q Okay. Got that.</p> <p>24 Okay. Let me show you what we'll have</p> <p>25 marked as Exhibit 28.</p>
Page 395	Page 397
<p>1 mortality studies of women with heavy occupational</p> <p>2 exposure to asbestos."</p> <p>3 Do you see that?</p> <p>4 A I do.</p> <p>5 Q Okay. And then if you go -- and then it</p> <p>6 cites those studies.</p> <p>7 Do you see that?</p> <p>8 A I do.</p> <p>9 Q And go down to where it starts: "The</p> <p>10 working group carefully considered the</p> <p>11 possibilities that cases of peritoneal</p> <p>12 mesothelioma may have been misdiagnosed as ovarian</p> <p>13 cancer, and that these contributed to the observed</p> <p>14 excesses."</p> <p>15 Do you see that?</p> <p>16 A I do.</p> <p>17 Q Okay. Did I read that correctly?</p> <p>18 A Yes.</p> <p>19 Q Okay. In your report you stated that it</p> <p>20 was your belief that perhaps the results were</p> <p>21 limited by virtue of the fact that there may have</p> <p>22 been misdiagnosis between peritoneal mesothelioma</p> <p>23 and ovarian cancer cases.</p> <p>24 Do you remember writing that?</p> <p>25 A I do.</p>	<p>1 (Diette Exhibit No. 28 was marked</p> <p>2 for identification.)</p> <p>3 BY MS. PARFITT:</p> <p>4 Q Okay. Diette Exhibit 28, if you will.</p> <p>5 There you go.</p> <p>6 MS. PARFITT: And, Counsel, I have a</p> <p>7 copy for you.</p> <p>8 MS. BROWN: Thank you.</p> <p>9 MS. PARFITT: Of course.</p> <p>10 Sorry, guys. I'm going to need one.</p> <p>11 I'm sorry. I'll give you this one later.</p> <p>12 BY MS. PARFITT:</p> <p>13 Q Okay. I will represent to you that that</p> <p>14 is -- that is Table 2.8, which is referenced in</p> <p>15 the IARC report on page 253 and 254.</p> <p>16 And it says: "Epidemiological studies</p> <p>17 of asbestos exposure and ovarian cancer," and then</p> <p>18 in parens, "and for comparison, lung cancer and</p> <p>19 mesothelioma."</p> <p>20 Do you see that?</p> <p>21 A I do.</p> <p>22 Q All right. Look over at the first study</p> <p>23 mentioned there, the Atkinson study from 1982.</p> <p>24 A Mm-hmm.</p> <p>25 Q All right. Do you see that the relative</p>

Gregory B. Diette, M.D.

Page 398	Page 400
<p>1 risk for ovarian cancer and lung cancer, for 2 ovarian cancer it was 2.75, and for lung cancer it 3 was 2.41. Do you see that? 4 A I do. 5 Q Okay. Then move down to the Wignall and 6 Fox study. It's a 1982 study. Do you see that? 7 A I don't -- oh, yeah, the next one down, 8 yeah. 9 Q Okay, yeah. Do you see that the 10 relative risk for ovarian cancer were 2.13, and 11 for lung cancer 2.73? 12 A Correct. 13 Q And let's move down to Pira in 2005. Do 14 you see where the relative risk for ovarian cancer 15 were 2.61 and for lung cancer 2.82? 16 A I do. 17 Q All right. And then let's move to 18 Magnani, a 2008 study. 19 All right. Do you see -- and this is 20 one of the studies that the working group of IARC 21 looked at. They determined that the relative risk 22 for -- not determined -- they indicated that the 23 relative risk for ovarian cancer on the Magnani 24 study was 2.27, and for lung cancer 2.20. 25 Do you see that?</p>	<p>1 BY MS. PARFITT: 2 Q Sure. 3 A In one of your questions a little while 4 back, you were asking me to agree that you were 5 reading fine, and you were for the relative risks. 6 Q Yeah. 7 A None of these are relative risks, 8 though. They're SMRs and SIRs. So just a 9 slightly different -- 10 Q I appreciate that. Thank you. Thank 11 you for the correction. Thank you. 12 Next question. Do you intend to give an 13 opinion that fibrous talc is a carcinogen? 14 MS. BROWN: Form. 15 THE WITNESS: I'm not sure I understand 16 what fibrous talc is. 17 BY MS. PARFITT: 18 Q Okay. Let me direct your attention 19 to -- we'll go back to the IARC on ovarian 20 cancer -- or, excuse me, IARC on asbestos. 21 Paragraph 1.1 on page 219. 22 Are you there? 23 A Paragraph 1, yes. 24 Q Yes. Okay. Do you see where after it 25 has IARC, '73, and USGS, 2001, it states: "The</p>
Page 399	Page 401
<p>1 A I do. 2 Q All right. And let's go on to the 3 Ferrante study. Do you see that? 4 MS. BROWN: Where -- where are you? 5 MS. PARFITT: On the last page. 6 BY MS. PARFITT: 7 Q Do you see that? It's on the last page, 8 Ferrante, 2007. Do you see that? 9 A I do. 10 Q Okay. And the relative risk for ovarian 11 cancer was 1.43, and for lung cancer it was 1.17. 12 Now, I'll represent to you, Doctor -- 13 or, Dr. Diette, is it fair to say that this 14 Table 2.8 of epidemiological exposures, asbestos 15 exposure and ovarian cancer formed part of the 16 bases for IARC's decision in their IARC report 17 that asbestos -- or ovarian -- asbestos causes 18 ovarian cancer? 19 A I assume so, yeah. 20 Q Okay. All right. Let's talk a little 21 bit -- do you intend to give an opinion in this 22 case that fibrous talc is a carcinogen? 23 MS. BROWN: Objection to the form. 24 THE WITNESS: I just want to correct 25 something real quick.</p>	<p>1 conclusions reached in this monograph about 2 asbestos and its carcinogenic risks apply to these 3 six types of fibres wherever they are found, and 4 that includes talc containing asbestiform fibres." 5 Do you see that? 6 A Yes. 7 Q All right. Do you intend to give an 8 opinion in this case that talc containing 9 asbestiform fibers can cause ovarian cancer? 10 MS. BROWN: Objection to the form. 11 That's different than the original question. 12 MS. PARFITT: It is. 13 MS. BROWN: Did you mean it to be? 14 MS. PARFITT: No. I mean the new 15 question. 16 MS. BROWN: Okay. 17 THE WITNESS: So, because to me, the way 18 I have read this before and then also again now, I 19 think, although I can't know what they were 20 intending, but this to me says basically talc with 21 asbestos in it -- what we would agree is talc with 22 asbestos in it, as opposed to something else. 23 And I don't think you need the "talc 24 containing." I think you could say anything 25 containing asbestos, you know, could potentially</p>

101 (Pages 398 to 401)

Gregory B. Diette, M.D.

Page 402	Page 404
<p>1 increase carcinogenic risk if there's enough of a 2 dose. 3 BY MS. PARFITT: 4 Q Okay. Did you see anywhere in the IARC 5 working group document that we've been talking 6 about that the working group determined that there 7 was a causal association between asbestos and 8 ovarian cancer, but it depended on the dose? 9 MR. LOCKE: Objection. 10 MS. BROWN: Objection to the form of the 11 question. 12 THE WITNESS: I don't recall. 13 BY MS. PARFITT: 14 Q Okay. You've worked an secondhand smoke 15 studies, correct? 16 A Yes. 17 Q How do you determine the dose for those? 18 MS. BROWN: Objection to the form. 19 THE WITNESS: So the dose of secondhand 20 smoke? 21 BY MS. PARFITT: 22 Q Mm-hmm. 23 A So it depends, right. So at the moment, 24 it -- so it depends upon which kind of study. And 25 when you say "you," do you mean you in the broad</p>	<p>1 sufficient dose. It's not a measurement of dose. 2 It's an indicator of sufficient -- sufficient 3 exposure to be linkable to things like lung 4 cancer. 5 The same kind of question for being 6 around coworkers, and so a yes/no to that has been 7 sufficient. 8 In our other studies, we -- we get more 9 precise so that we'll -- and use a variety of 10 overlapping methods. So one is to -- to query -- 11 if it's a child study, to query the parent about 12 the number of cigarettes that are smoked per day 13 in the home, and with a very elaborate procedure 14 of asking not only the person who is answering the 15 questionnaire but about all the other people that 16 are in and out of the house that day, so we get a 17 count of cigarettes. 18 We also use different types of 19 particulate matter monitors, and we've established 20 that you can estimate about 1 microgram per meter 21 cubed of particulate matter per cigarette smoked 22 in the home. So we've got an estimate that way. 23 We -- we collect nicotine and cotinine 24 from a variety of sources, so we've collected 25 hair, saliva, urine, and blood. And so depending</p>
Page 403	Page 405
<p>1 sense or me, Greg Diette? 2 Q Well, Greg Diette has been doing 3 research on secondhand smoke, and you, Greg 4 Diette, has indicated that dose is important to 5 you. So what I'd like to know is how you measure 6 the dose in your secondhand smoke. 7 A Yeah, so a lot of different -- 8 MS. BROWN: Objection. Dose is 9 important to him as it relates to secondhand 10 smoke, is that what the question is asking? 11 MS. PARFITT: No. 12 BY MS. PARFITT: 13 Q I was just reiterating that you, 14 Dr. Diette, have done several secondhand smoke 15 studies, correct? 16 A Yes. 17 Q Okay. And how do you measure the dose 18 in the studies that you have performed? 19 A So different ways, depending upon the 20 studies. So for some studies, it's simple enough 21 to ask, especially if you're talking about an 22 adult, whether or not they've had secondhand smoke 23 exposure from their parents, often broken down by 24 whether it's mother or father. And for some -- 25 some studies, that's a sufficient indicator of a</p>	<p>1 upon which study and which population, we can 2 estimate something about dose based on what 3 their -- what their sort of biomarker is. 4 Q All right. How much have you -- 5 understanding those metrics, for lack of a better 6 word, how much smoke does a patient need to 7 actually inhale? 8 MS. BROWN: For what? 9 BY MS. PARFITT: 10 Q In order to determine whether or not 11 they have been impacted by secondhand smoke. 12 MS. BROWN: Objection to the form. 13 THE WITNESS: That's a complicated 14 question, I guess, because we don't -- at least in 15 our studies, we don't measure -- like I don't know 16 what that means, like how much they inhale. I can 17 tell you, you know, what their absorbed dose is of 18 nicotine, right, which has some implication about 19 how much they might have inhaled, but I don't 20 relate that to like sort of a volume of smokey air 21 or something like that, the way that you might if 22 you were doing like a smoke machine, you know, 23 study. 24 So it's really -- it's implied, right. 25 If you find it in the urine and the blood, they</p>

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 406</p> <p>1 inhaled it enough in order to get that particular</p> <p>2 fluid level high enough to -- for you to measure</p> <p>3 it. And same with saliva and same with hair.</p> <p>4 BY MS. PARFITT:</p> <p>5 Q Okay.</p> <p>6 A I left one out too. We also measure</p> <p>7 airborne nicotine, and so that's another</p> <p>8 indicator. So I was talking about cotinine that's</p> <p>9 measured in -- in the people, but we also have</p> <p>10 nicotine matches, and we'll measure nicotine</p> <p>11 directly in the environment.</p> <p>12 Q Based upon -- I meant to ask this</p> <p>13 earlier. Based upon your study of ovarian cancer</p> <p>14 and talcum powder products that you've done for</p> <p>15 Johnson & Johnson, have you made any of these</p> <p>16 recommendations to Johnson & Johnson as to how --</p> <p>17 what kind of study they could perform in order to</p> <p>18 ascertain dose?</p> <p>19 MS. BROWN: What?</p> <p>20 MR. LOCKE: Objection.</p> <p>21 MS. BROWN: Objection to the form of the</p> <p>22 question.</p> <p>23 BY MS. PARFITT:</p> <p>24 Q Let me ask it again.</p> <p>25 A Oh, no, I heard it. I was just -- I</p>	<p style="text-align: right;">Page 408</p> <p>1 couple-year study and, you know, tens of thousands</p> <p>2 of dollars spent doing it?</p> <p>3 MR. LOCKE: Objection.</p> <p>4 MS. BROWN: Objection to the form.</p> <p>5 There are multiple questions in there, Counsel.</p> <p>6 Can you rephrase?</p> <p>7 BY MS. PARFITT:</p> <p>8 Q Do you understand the question?</p> <p>9 A The -- the last part you said -- I'll</p> <p>10 try to paraphrase it so we know we're talking</p> <p>11 about the same thing. I have not -- I have not</p> <p>12 done anything to inform the medical community</p> <p>13 about the findings so far from my -- you know,</p> <p>14 from my work on these cases.</p> <p>15 Q Do you intend to do so?</p> <p>16 A I don't have any active intention to do</p> <p>17 it right now.</p> <p>18 Q Okay. Do you intend to have your report</p> <p>19 peer -- published?</p> <p>20 A It's not in the right format for that.</p> <p>21 Q Okay. Do you intend to do any</p> <p>22 meta-analysis of your work?</p> <p>23 MS. BROWN: Objection to the form.</p> <p>24 THE WITNESS: Not on that -- not on that</p> <p>25 topic.</p>
<p style="text-align: right;">Page 407</p> <p>1 guess the broad answer is no. I mean I haven't</p> <p>2 made any recommendations about studies to Johnson</p> <p>3 & Johnson for -- for anything.</p> <p>4 Q Okay. And the reason I ask is, your</p> <p>5 work appears to be reviewing and surveying the</p> <p>6 literature for Johnson & Johnson in order to give</p> <p>7 litigation opinions on whether or not talcum</p> <p>8 powder products can cause ovarian cancer.</p> <p>9 MR. LOCKE: Objection.</p> <p>10 MS. BROWN: Objection to the form of the</p> <p>11 question.</p> <p>12 BY MS. PARFITT:</p> <p>13 Q Correct?</p> <p>14 A Can you say it again?</p> <p>15 Q Sure.</p> <p>16 A I spaced out a little bit.</p> <p>17 Q No, that's all right. It's getting late</p> <p>18 in the day.</p> <p>19 Your work for Johnson & Johnson appears</p> <p>20 to be surveying the literature, preparing</p> <p>21 litigation reports, and then giving testimony in a</p> <p>22 court that the Johnson & Johnson product is safe.</p> <p>23 And my question for you is, what have</p> <p>24 you done in order to inform the scientific</p> <p>25 community of the results of your -- your now</p>	<p style="text-align: right;">Page 409</p> <p>1 BY MS. PARFITT:</p> <p>2 Q Okay. And if you saw with regard to</p> <p>3 Health Canada, they have given -- they gave</p> <p>4 individuals an opportunity to comment on the work</p> <p>5 that they did and present that to them.</p> <p>6 You saw that, correct?</p> <p>7 A Yes.</p> <p>8 Q Okay. So you had an opportunity as</p> <p>9 someone who's reviewed the literature to write to</p> <p>10 Health Canada and inform them of your concern</p> <p>11 about the manner in which they conducted their</p> <p>12 study. Fair?</p> <p>13 MS. BROWN: Objection to the form, lacks</p> <p>14 foundation.</p> <p>15 THE WITNESS: I guess. I actually don't</p> <p>16 know who they're asking. Like I haven't looked to</p> <p>17 see whether they're looking for people outside of</p> <p>18 Canada.</p> <p>19 I don't even know who they are. I mean</p> <p>20 the only reason I've heard of Health Canada is</p> <p>21 because of this litigation and because something,</p> <p>22 you know, opportunistic came up. But otherwise, I</p> <p>23 mean I wouldn't be talking to Health Canada about</p> <p>24 anything or reading whatever they've written.</p> <p>25 BY MS. PARFITT:</p>

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 410</p> <p>1 Q Something opportunist came up. Is that</p> <p>2 the fact that you are being engaged in this</p> <p>3 litigation --</p> <p>4 A No.</p> <p>5 MS. BROWN: Objection --</p> <p>6 BY MS. PARFITT:</p> <p>7 Q -- as an expert witness?</p> <p>8 MS. BROWN: Objection to the form.</p> <p>9 THE WITNESS: Oh, no, I just see -- I</p> <p>10 think the reason that I have it in front of me is</p> <p>11 because it -- it seemed to help -- help</p> <p>12 plaintiffs' experts to be able to say something</p> <p>13 else about this -- this story. And if -- if it</p> <p>14 had said something else, then I probably wouldn't</p> <p>15 even have heard about it.</p> <p>16 BY MS. PARFITT:</p> <p>17 Q Okay. This story, Dr. Diette, is about</p> <p>18 women who are dying of ovarian cancer --</p> <p>19 MS. BROWN: Careful -- what's the</p> <p>20 question?</p> <p>21 BY MS. PARFITT:</p> <p>22 Q -- having been exposed to talcum powder</p> <p>23 products.</p> <p>24 Do you understand that?</p> <p>25 MR. LOCKE: Objection.</p>	<p style="text-align: right;">Page 412</p> <p>1 MS. BROWN: Objection.</p> <p>2 THE WITNESS: The only studies I've seen</p> <p>3 are the ones that -- I think that were cited by --</p> <p>4 by IARC with -- if that's what we're talking</p> <p>5 about, is like women who were about to have</p> <p>6 surgery for some other reason and -- and different</p> <p>7 things placed either in their uterus or vagina,</p> <p>8 although not necessarily talc. I mean all kinds</p> <p>9 of things, you know, carbon particles,</p> <p>10 radiolabeled particles, different things that</p> <p>11 aren't talc.</p> <p>12 (Counsel conferring.)</p> <p>13 BY MS. PARFITT:</p> <p>14 Q So sitting here today, is it your</p> <p>15 testimony that you have not reviewed or seen in</p> <p>16 the medical literature that particles of talc can</p> <p>17 migrate to the ovaries, lymph nodes, of a woman's</p> <p>18 body?</p> <p>19 MS. BROWN: Objection to the form of the</p> <p>20 question.</p> <p>21 MR. LOCKE: Objection.</p> <p>22 THE WITNESS: So -- so the study would</p> <p>23 be one where somebody applied talc to the perineum</p> <p>24 and then demonstrated that it migrated from there</p> <p>25 to the ovaries or into some lymph node somewhere?</p>
<p style="text-align: right;">Page 411</p> <p>1 MS. BROWN: Objection to the form of the</p> <p>2 question.</p> <p>3 THE WITNESS: I understand the general</p> <p>4 notion is about ovarian cancer and whether there</p> <p>5 is or is not a risk from talcum powder.</p> <p>6 BY MS. PARFITT:</p> <p>7 Q I appreciate that.</p> <p>8 All right, Dr. Diette, do you agree that</p> <p>9 there is scientific evidence published in the</p> <p>10 peer-reviewed journal that talcum powder products</p> <p>11 can migrate from the vagina to the peritoneal</p> <p>12 capacity up through the ovaries?</p> <p>13 MS. BROWN: Objection to the form.</p> <p>14 MR. LOCKE: Objection.</p> <p>15 THE WITNESS: From the perineum?</p> <p>16 BY MS. PARFITT:</p> <p>17 Q From the perineum.</p> <p>18 MS. BROWN: Objection.</p> <p>19 THE WITNESS: I have not seen that.</p> <p>20 BY MS. PARFITT:</p> <p>21 Q Okay. Do you have -- have you seen in</p> <p>22 your review of the literature that talcum powder</p> <p>23 products can migrate from the vagina to the</p> <p>24 ovaries?</p> <p>25 MR. LOCKE: Objection.</p>	<p style="text-align: right;">Page 413</p> <p>1 BY MS. PARFITT:</p> <p>2 Q That's right.</p> <p>3 A I have not seen that study.</p> <p>4 Q Okay. You've read the Schildkraut</p> <p>5 study, correct?</p> <p>6 A Yes.</p> <p>7 Q Okay. Do you agree with the authors of</p> <p>8 the Schildkraut study that chronic inflammation</p> <p>9 resulting from the use of exposure to baby powder,</p> <p>10 whether through inhalation or through a</p> <p>11 transvaginal route, may lead to an increased risk</p> <p>12 of ovarian cancer?</p> <p>13 MR. LOCKE: Objection.</p> <p>14 MS. BROWN: Objection to the form of the</p> <p>15 question.</p> <p>16 THE WITNESS: I've read the study. I'd</p> <p>17 like to see whether that's in the introduction or</p> <p>18 the conclusion.</p> <p>19 BY MS. PARFITT:</p> <p>20 Q Okay. Let me show you Schildkraut.</p> <p>21 A Because it's certainly not a conclusion</p> <p>22 of their study.</p> <p>23 (Diette Exhibit No. 29 was marked</p> <p>24 for identification.)</p> <p>25 MS. BROWN: Do you guys want a number on</p>

104 (Pages 410 to 413)

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 414</p> <p>1 this?</p> <p>2 MS. PARFITT: Sure. What number are we</p> <p>3 up to?</p> <p>4 MS. BROWN: Oh, 29. I'm sorry. It's</p> <p>5 there. My bad.</p> <p>6 BY MS. PARFITT:</p> <p>7 Q Do you have that in front of you,</p> <p>8 Doctor?</p> <p>9 A I do.</p> <p>10 Q Okay. And if I can direct your</p> <p>11 attention to pages 14, 16.</p> <p>12 A Got you.</p> <p>13 Q Do you have that?</p> <p>14 Do you see where the authors state:</p> <p>15 "Lung inhalation of powder could be a biologically</p> <p>16 plausible mechanism for the association between</p> <p>17 nongenital powder use and increased EOC risk,</p> <p>18 particularly non-serous EOC."</p> <p>19 Do you see that?</p> <p>20 A I do. It's the top of the first column</p> <p>21 in the -- the rest of the incomplete paragraph.</p> <p>22 Q Okay. Do you see that?</p> <p>23 A I do.</p> <p>24 Q Okay. Do you agree with that?</p> <p>25 MR. LOCKE: Objection.</p>	<p style="text-align: right;">Page 416</p> <p>1 MR. LOCKE: Objection.</p> <p>2 BY MS. PARFITT:</p> <p>3 Q Okay. Do you agree that there is</p> <p>4 reliable scientific literature in the</p> <p>5 peer-reviewed studies to support that it is</p> <p>6 biologically plausible for talc products to</p> <p>7 migrate from the vagina to the ovaries following</p> <p>8 perineal application?</p> <p>9 A I'm not aware of that study that has</p> <p>10 shown that.</p> <p>11 Q Have you seen the Penninkilampi study?</p> <p>12 A Oh.</p> <p>13 MS. BROWN: Objection.</p> <p>14 THE WITNESS: Yes, I have.</p> <p>15 BY MS. PARFITT:</p> <p>16 Q Okay. Why don't we take a look at that.</p> <p>17 Let's pull it up, and we'll make it</p> <p>18 Exhibit No. 30.</p> <p>19 (Diette Exhibit No. 30 was marked</p> <p>20 for identification.)</p> <p>21 BY MS. PARFITT:</p> <p>22 Q Right here. And if I may, Doctor, let</p> <p>23 me direct your attention to the discussion section</p> <p>24 of Penninkilampi on page 45.</p> <p>25 A Page 45?</p>
<p style="text-align: right;">Page 415</p> <p>1 THE WITNESS: Only -- well, no. Only in</p> <p>2 the broadest sense that lots of things could be,</p> <p>3 but not because there's any evidence to show that</p> <p>4 inhalation of powder is a way to get to the</p> <p>5 ovaries.</p> <p>6 BY MS. PARFITT:</p> <p>7 Q All right. So you dispute that</p> <p>8 inhalation of talcum powder products can cause</p> <p>9 ovarian cancer. Is that your testimony?</p> <p>10 A Inhalation?</p> <p>11 Q Inhalation.</p> <p>12 A I haven't seen any evidence that it can.</p> <p>13 I mean there's not affirmative evidence to say</p> <p>14 that it absolutely can't, but there's no evidence</p> <p>15 that there's been talcum powder inhaled, leading</p> <p>16 to other -- other diseases along the way, and I</p> <p>17 haven't seen any study that has shown that it can</p> <p>18 migrate from the lungs to the ovaries. And so --</p> <p>19 I mean people could say that, but it's not based</p> <p>20 on -- on studies.</p> <p>21 Q Does the fact that talcum powder</p> <p>22 products can be inhaled support a biologically</p> <p>23 plausible mechanism for talcum powder products to</p> <p>24 cause ovarian cancer?</p> <p>25 A No.</p>	<p style="text-align: right;">Page 417</p> <p>1 Q 45.</p> <p>2 A Yep.</p> <p>3 Q Do you have that?</p> <p>4 A I'm there, yep.</p> <p>5 Q Okay. It says: "The present</p> <p>6 meta-analysis" -- and it is meta-analysis,</p> <p>7 correct?</p> <p>8 A Yeah, part of this study is a</p> <p>9 meta-analysis.</p> <p>10 Q "The present meta-analysis reports a</p> <p>11 positive association between perineal talc use and</p> <p>12 ovarian cancer, specifically of the serous and</p> <p>13 endometriode -- and endometrioid histology site --</p> <p>14 subtypes. The mechanism by which perineal talc</p> <p>15 use may increase the risk of ovarian cancer is</p> <p>16 uncertain. It has been previously proposed that</p> <p>17 talc as a foreign body may ascend from the vagina</p> <p>18 through to the uterine tubes and instigate a</p> <p>19 chronic inflammatory response, which may</p> <p>20 predispose to the development of ovarian cancer."</p> <p>21 Did I read that correctly?</p> <p>22 A You did.</p> <p>23 Q Okay. Do you agree with that?</p> <p>24 MR. LOCKE: Objection.</p> <p>25 MS. BROWN: Objection to the form.</p>

105 (Pages 414 to 417)

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 418</p> <p>1 THE WITNESS: So -- so I agree with a</p> <p>2 lot of this, right. So I agree that the mechanism</p> <p>3 is uncertain. Right. I agree that it has been</p> <p>4 previously proposed 20 years ago by the citation</p> <p>5 that they have that that may ascend from the</p> <p>6 vagina, and instigate a chronic inflammation</p> <p>7 response.</p> <p>8 They don't cite anything more modern</p> <p>9 than that one from 20 years ago, though. And</p> <p>10 where it talks about it may be mutagenic and</p> <p>11 promote carcinogenesis --</p> <p>12 BY MS. PARFITT:</p> <p>13 Q Correct.</p> <p>14 A -- I don't -- I don't think that's well</p> <p>15 supported either.</p> <p>16 Q Is migration of talc a biologically</p> <p>17 plausible mechanism by which talc can reach the</p> <p>18 ovaries?</p> <p>19 MS. BROWN: Objection to the form.</p> <p>20 MR. LOCKE: Objection.</p> <p>21 THE WITNESS: If it were true, it could</p> <p>22 be supportive of that. But I don't see any -- any</p> <p>23 evidence that it's true.</p> <p>24 BY MS. PARFITT:</p> <p>25 Q Is biological plausibility essential for</p>	<p style="text-align: right;">Page 420</p> <p>1 inflammatory hypothesis, as repeated exposure</p> <p>2 would induce a longer period of chronic</p> <p>3 inflammation, and therefore should increase the</p> <p>4 predisposition to the development of ovarian</p> <p>5 cancer."</p> <p>6 Did I read that correctly?</p> <p>7 A You did.</p> <p>8 Q All right. Do you agree with that</p> <p>9 statement, that chronic inflammation as a</p> <p>10 biologically plausible hypothesis could induce</p> <p>11 carcinogenicity?</p> <p>12 MR. LOCKE: Objection.</p> <p>13 MS. BROWN: Counsel, are you</p> <p>14 intentionally not reading the rest of that</p> <p>15 paragraph?</p> <p>16 MS. PARFITT: No, I -- I'm getting</p> <p>17 there.</p> <p>18 MS. BROWN: Okay.</p> <p>19 MS. PARFITT: Yeah.</p> <p>20 THE WITNESS: Well, I disagree with the</p> <p>21 fact that the small difference between 3600, plus</p> <p>22 or minus, lifetime applications supports a -- an</p> <p>23 inflammatory theory, because that's got nothing</p> <p>24 too do with inflammation. It's really just a -- a</p> <p>25 total number of applications.</p>
<p style="text-align: right;">Page 419</p> <p>1 causality?</p> <p>2 A No, it's -- it's one important criterion</p> <p>3 to consider.</p> <p>4 Q Does biological plausibility mean it</p> <p>5 must be proved?</p> <p>6 MS. BROWN: Objection.</p> <p>7 THE WITNESS: And I assume we're talking</p> <p>8 about in the context of a Bradford Hill?</p> <p>9 BY MS. PARFITT:</p> <p>10 Q Correct.</p> <p>11 A Yeah, so -- so the answer is, no, it</p> <p>12 doesn't have to be proved.</p> <p>13 Q Look at the lower right-hand corner of</p> <p>14 that article.</p> <p>15 MS. BROWN: Are we done with that</p> <p>16 paragraph, Counsel?</p> <p>17 MS. PARFITT: We are. Thank you very</p> <p>18 much, yeah.</p> <p>19 BY MS. PARFITT:</p> <p>20 Q And if you will go down to the lower</p> <p>21 right, it starts with "We also found."</p> <p>22 A Okay.</p> <p>23 Q Do you see that?</p> <p>24 Okay. It says: "This finding also</p> <p>25 supports the chronic" -- I'm sorry -- "chronic</p>	<p style="text-align: right;">Page 421</p> <p>1 BY MS. PARFITT:</p> <p>2 Q Perhaps I can simplify my answer. Do</p> <p>3 you have an opinion as to whether or not chronic</p> <p>4 inflammation can be a biologically plausible</p> <p>5 method for promoting carcinogenesis?</p> <p>6 MS. BROWN: Objection to the form.</p> <p>7 THE WITNESS: In -- in all kinds of</p> <p>8 cancer or ovarian cancer?</p> <p>9 BY MS. PARFITT:</p> <p>10 Q In ovarian cancer.</p> <p>11 A So I -- I don't think there's strong</p> <p>12 evidence to support that.</p> <p>13 Q Is there evidence at all?</p> <p>14 MS. BROWN: Let him finish.</p> <p>15 THE WITNESS: So not much. I mean</p> <p>16 there's -- I know that folks have looked at, you</p> <p>17 know, whether NSAIDS and aspirin, whether that use</p> <p>18 would lead to a limitation in risk, and it seems</p> <p>19 like the -- the findings are kind of mixed. And</p> <p>20 sometimes aspirin in a particular dose is</p> <p>21 protective and aspirin of another dose is not.</p> <p>22 That NSAIDS are sometimes protective, but mostly</p> <p>23 not.</p> <p>24 Since preparing my report, I saw</p> <p>25 Dr. Shih -- Shih's report talking about the stick</p>

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 422</p> <p>1 cells, like these precursor cells, and -- and at</p> <p>2 least, you know, from histologic specimens, not</p> <p>3 seeing evidence of inflammation. And I haven't</p> <p>4 really seen much that -- that would confirm that</p> <p>5 there's a link between chronic inflammation.</p> <p>6 BY MS. PARFITT:</p> <p>7 Q What I'm asking you is, based upon your</p> <p>8 review, Dr. Diette, have you seen anything in the</p> <p>9 peer-reviewed literature that there are</p> <p>10 biologically plausible mechanisms of talc's</p> <p>11 carcinogenicity demonstrated by chronic</p> <p>12 inflammation from migration of the talc to the</p> <p>13 ovaries?</p> <p>14 MS. BROWN: Objection. I don't</p> <p>15 understand that question.</p> <p>16 MR. LOCKE: Objection.</p> <p>17 THE WITNESS: Would you --</p> <p>18 BY MS. PARFITT:</p> <p>19 Q The question -- let me rephrase it.</p> <p>20 A Okay.</p> <p>21 Q Is there -- are there studies in the</p> <p>22 peer-reviewed literature that support an</p> <p>23 association of inflammation and increased risk of</p> <p>24 ovarian cancer?</p> <p>25 MS. BROWN: Objection to the form, asked</p>	<p style="text-align: right;">Page 424</p> <p>1 BY MS. PARFITT:</p> <p>2 Q T-A-H-E-R.</p> <p>3 A Oh.</p> <p>4 Q 2018.</p> <p>5 A Sorry, I was saying Taher.</p> <p>6 Q No, no problem.</p> <p>7 A But I don't now how you --</p> <p>8 Q You could be right on that. Probably</p> <p>9 are.</p> <p>10 A I don't know.</p> <p>11 I did.</p> <p>12 Q Do you see where Taher authors found</p> <p>13 that there was biologically plausible evidence of</p> <p>14 inflammation from talc exposure?</p> <p>15 MS. BROWN: Objection. Counsel, can we</p> <p>16 see the article if you want to ask him about it?</p> <p>17 MR. LOCKE: Objection.</p> <p>18 BY MS. PARFITT:</p> <p>19 Q You've read the article. Do you know</p> <p>20 the answer to that?</p> <p>21 MS. BROWN: But it's not a memory test.</p> <p>22 MS. PARFITT: No, it's not, but perhaps</p> <p>23 he can answer. I didn't ask you the question.</p> <p>24 BY MS. PARFITT:</p> <p>25 Q Do you know the answer to that?</p>
<p style="text-align: right;">Page 423</p> <p>1 and answered.</p> <p>2 BY MS. PARFITT:</p> <p>3 Q Is there something in the literature?</p> <p>4 MS. BROWN: Objection.</p> <p>5 BY MS. PARFITT:</p> <p>6 Q Not whether there is a lot or a little.</p> <p>7 Is there anything in the peer-reviewed literature</p> <p>8 that you've seen that supports an association</p> <p>9 between inflammation and an increased risk of</p> <p>10 ovarian cancer?</p> <p>11 MS. BROWN: Objection to the form.</p> <p>12 THE WITNESS: I've seen the paper where</p> <p>13 C-reactive protein in the serum popped out of</p> <p>14 dozens of different markers of inflammation and</p> <p>15 predated the diagnosis of ovarian cancer.</p> <p>16 I guess I haven't really seen something</p> <p>17 that shows that chronic inflammation in the</p> <p>18 ovaries is -- is a precursor to ovarian cancer or</p> <p>19 that talc induces that particular chronic</p> <p>20 inflammation that would in turn lead to cancer.</p> <p>21 BY MS. PARFITT:</p> <p>22 Q Have you read Taher? You've read the</p> <p>23 Taher study, correct?</p> <p>24 MR. LOCKE: Objection.</p> <p>25 THE WITNESS: How do you spell it?</p>	<p style="text-align: right;">Page 425</p> <p>1 A Well, the paper wasn't about that, so I</p> <p>2 don't -- I don't remember whether there was sort</p> <p>3 of a preamble thing, but they -- they weren't</p> <p>4 really analyzing that. They were doing a</p> <p>5 meta-analysis, you know, sort of combining the epi</p> <p>6 studies. So, I mean, I don't remember what their</p> <p>7 statement was, but when you --</p> <p>8 Q All right. Did you --</p> <p>9 A I'm sorry, I just want to say, but if</p> <p>10 you say that they found it, by finding it, I don't</p> <p>11 think they demonstrated it or it was a finding</p> <p>12 from their study per se.</p> <p>13 Q Okay. Have you read Langseth, 2008?</p> <p>14 A Langseth, 2008?</p> <p>15 Q Correct.</p> <p>16 A Is that a meta-analysis?</p> <p>17 Q Correct.</p> <p>18 A Yes.</p> <p>19 Q All right. And do you see where the</p> <p>20 Langseth authors also found migration and -- and</p> <p>21 concluded that there was chronic inflammation that</p> <p>22 was biologically plausible?</p> <p>23 MS. BROWN: No, I -- I object. If</p> <p>24 you're going to quote articles --</p> <p>25 BY MS. PARFITT:</p>

107 (Pages 422 to 425)

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 426</p> <p>1 Q Do you remember?</p> <p>2 MS. BROWN: -- I would request the</p> <p>3 article.</p> <p>4 MS. PARFITT: I can do that.</p> <p>5 BY MS. PARFITT:</p> <p>6 Q Do you know, Doctor?</p> <p>7 A I don't remember what they said.</p> <p>8 (Counsel conferring.)</p> <p>9 MS. PARFITT: Doctor, if we can take a</p> <p>10 quick break here --</p> <p>11 THE WITNESS: Sure.</p> <p>12 MS. PARFITT: -- right now, so maybe I</p> <p>13 can --</p> <p>14 THE WITNESS: Yeah, it's a good time.</p> <p>15 MS. PARFITT: -- shorten things.</p> <p>16 THE VIDEOGRAPHER: The time is 4:59 p.m.</p> <p>17 We're going off the record.</p> <p>18 (Recess.)</p> <p>19 THE VIDEOGRAPHER: The time is 5:12 p.m.</p> <p>20 and we're back on the record.</p> <p>21 MS. PARFITT: I apologize.</p> <p>22 BY MS. PARFITT:</p> <p>23 Q Dr. Diette, and I apologize, I have only</p> <p>24 one copy that isn't marked up, so we're going to</p> <p>25 have to put this and substitute it on the -- on</p>	<p style="text-align: right;">Page 428</p> <p>1 He doesn't have the article.</p> <p>2 MS. PARFITT: That's fine.</p> <p>3 MS. BROWN: And he's never read it.</p> <p>4 BY MS. PARFITT:</p> <p>5 Q Look at the abstract, first sentence.</p> <p>6 It says: "Perineal talc use is associated with</p> <p>7 ovarian carcinoma in many case-control studies.</p> <p>8 Such talc may migrate to pelvic organs and</p> <p>9 regional lymph nodes, with both clinical and legal</p> <p>10 significance."</p> <p>11 Did I read that correctly?</p> <p>12 A Yes.</p> <p>13 Q All right. Would it be -- I believe you</p> <p>14 had some concerns about the Heller study that we</p> <p>15 talked about earlier because it involved some</p> <p>16 unexposed -- what you testified were unexposed</p> <p>17 women.</p> <p>18 MS. BROWN: Objection to the form.</p> <p>19 THE WITNESS: Correct, women who</p> <p>20 reported not being perineal talc users.</p> <p>21 BY MS. PARFITT:</p> <p>22 Q Right. Okay. You understand in this</p> <p>23 study that what Drs. McDonald and Godleski were</p> <p>24 doing were looking at particles in exposed women.</p> <p>25 MS. BROWN: No, he doesn't understand</p>
<p style="text-align: right;">Page 427</p> <p>1 the ELMO, if I may. We've done pretty good with</p> <p>2 copies all day today.</p> <p>3 So here we go.</p> <p>4 MR. ROSEN: This will be Exhibit 31.</p> <p>5 (Diette Exhibit No. 31 was marked</p> <p>6 for identification.)</p> <p>7 BY MS. PARFITT:</p> <p>8 Q All right. Dr. Diette, this is an</p> <p>9 article from Ultrastructural Pathology, and it's</p> <p>10 entitled "Correlative polarizing light and</p> <p>11 scanning electron microscopy for the assessment of</p> <p>12 talc in pelvic region lymph nodes."</p> <p>13 Do you see that?</p> <p>14 A I do.</p> <p>15 Q And the lead author is Dr. McDonald,</p> <p>16 along with Cramer and Godleski, and others.</p> <p>17 Do you see that?</p> <p>18 A I do.</p> <p>19 Q All right. This is published in 2019.</p> <p>20 Have you had an opportunity to review</p> <p>21 this article?</p> <p>22 A I have not seen this one.</p> <p>23 Q Okay. I just have one question about</p> <p>24 it. And if --</p> <p>25 MS. BROWN: Well, I'm going to object.</p>	<p style="text-align: right;">Page 429</p> <p>1 that because he doesn't have the study and he</p> <p>2 hasn't read it. I object. It's not fair.</p> <p>3 THE WITNESS: I honestly have no idea</p> <p>4 what they've done.</p> <p>5 BY MS. PARFITT:</p> <p>6 Q Okay. Well, do you dispute that talc</p> <p>7 particles can migrate to the pelvic organs and</p> <p>8 regional lymph nodes?</p> <p>9 A I don't -- I don't know.</p> <p>10 MR. LOCKE: Asked and answered.</p> <p>11 BY MS. PARFITT:</p> <p>12 Q You don't know. You don't know. You</p> <p>13 don't know one way or another?</p> <p>14 MS. BROWN: Objection, misstates his</p> <p>15 private -- his prior testimony.</p> <p>16 THE WITNESS: Migrate from where to</p> <p>17 where? From --</p> <p>18 BY MS. PARFITT:</p> <p>19 Q It says right here: "Talc may migrate</p> <p>20 to pelvic organs and regional lymph nodes."</p> <p>21 MS. BROWN: Right, but he can't --</p> <p>22 THE WITNESS: Oh, I saw the "to," but I</p> <p>23 don't see the "from."</p> <p>24 BY MS. PARFITT:</p> <p>25 Q Does it make a difference to you?</p>

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 430</p> <p>1 MS. BROWN: Of course.</p> <p>2 BY MS. PARFITT:</p> <p>3 Q If it's from the vaginal area to the</p> <p>4 ovaries and the lymph nodes, does that make a</p> <p>5 difference whether --</p> <p>6 MR. LOCKE: Objection.</p> <p>7 MS. BROWN: Objection to the form, lacks</p> <p>8 foundation, calls for speculation about a document</p> <p>9 he told you he's never read.</p> <p>10 MR. LOCKE: Does the witness have a</p> <p>11 copy?</p> <p>12 MS. BROWN: No. That's the objection.</p> <p>13 MS. PARFITT: Tom, we didn't -- we only</p> <p>14 have one copy of it.</p> <p>15 MR. LOCKE: I think you need to disclose</p> <p>16 to the witness that three of these authors are</p> <p>17 paid experts, et cetera --</p> <p>18 MS. PARFITT: Tom, Tom, Tom, Tom.</p> <p>19 MR. LOCKE: Come on.</p> <p>20 MS. BROWN: No, but to be fair, you</p> <p>21 guys, if you want to ask him questions, he's got</p> <p>22 to look at it. I'm going to take it off the ELMO</p> <p>23 and give it to him if you're going to continue</p> <p>24 asking him questions.</p> <p>25 BY MS. PARFITT:</p>	<p style="text-align: right;">Page 432</p> <p>1 You had testified earlier that you</p> <p>2 disagree with Health Canada when they state that</p> <p>3 talc can migrate to the ovaries; is that correct?</p> <p>4 MR. LOCKE: Objection.</p> <p>5 MS. BROWN: Objection. Misstates prior</p> <p>6 testimony. I don't even think he said that.</p> <p>7 BY MS. PARFITT:</p> <p>8 Q Well, let me ask you. In the Health</p> <p>9 Canada report, they discuss the fact that it is</p> <p>10 biologically plausible for talc to migrate to the</p> <p>11 ovaries and then cause an inflammatory process.</p> <p>12 Do you agree or disagree with that?</p> <p>13 MR. LOCKE: Objection.</p> <p>14 MS. BROWN: Objection. Lacks</p> <p>15 foundation. Do you want to show him where they</p> <p>16 said that?</p> <p>17 THE WITNESS: I don't remember their</p> <p>18 statement about that.</p> <p>19 BY MS. PARFITT:</p> <p>20 Q You don't. Okay.</p> <p>21 How about this statement. Go down to --</p> <p>22 I believe it's -- one, two, three -- the third</p> <p>23 paragraph. Do you see that? It starts with</p> <p>24 "While."</p> <p>25 A No.</p>
<p style="text-align: right;">Page 431</p> <p>1 Q I'm not going to ask him any more</p> <p>2 questions on it, Doctor.</p> <p>3 A Okay. Thank you.</p> <p>4 Q All right. Let me show you --</p> <p>5 MR. LOCKE: Come on. Give him -- if</p> <p>6 you're going to give him -- if you're going to ask</p> <p>7 him about it --</p> <p>8 MR. TISI: You're not even on record.</p> <p>9 MS. PARFITT: Tom, it was just --</p> <p>10 MS. BROWN: Hey, hey, hey, guys. It's</p> <p>11 the end of the day.</p> <p>12 MS. PARFITT: Okay. Let's don't --</p> <p>13 MS. BROWN: Let's get through this.</p> <p>14 (Diette Exhibit No. 32 was marked</p> <p>15 for identification.)</p> <p>16 BY MS. PARFITT:</p> <p>17 Q 32. Let me show you what's been marked</p> <p>18 as Plaintiffs' Exhibit 32.</p> <p>19 I need a copy. There you go. Sorry.</p> <p>20 A Thank you.</p> <p>21 Q Okay. You previously testified that you</p> <p>22 -- take a look at it. You read this before, the</p> <p>23 FDA letter 2014?</p> <p>24 A I've seen this.</p> <p>25 Q Okay. Very good.</p>	<p style="text-align: right;">Page 433</p> <p>1 Q No?</p> <p>2 A Oh, I'm on a different page.</p> <p>3 Q I'm sorry. Page 5. Page 5.</p> <p>4 A Okay.</p> <p>5 Q Okay. "While there exists no direct</p> <p>6 proof of talc and ovarian carcinogenesis, the</p> <p>7 potential for particles to migrate from the</p> <p>8 perineum into the vagina to the peritoneal cavity</p> <p>9 is indisputable."</p> <p>10 Do you see that?</p> <p>11 A I do.</p> <p>12 Q Okay. Do you agree with the FDA?</p> <p>13 MS. BROWN: Objection to the form.</p> <p>14 THE WITNESS: So there's no citation for</p> <p>15 that. I don't know how they get -- I mean I don't</p> <p>16 know why they make that statement, and I -- it</p> <p>17 certainly doesn't seem to be indisputable, because</p> <p>18 there -- several of the articles that we've looked</p> <p>19 at today and others say it's not clear what the</p> <p>20 mechanism is or the biologic plausibility. So</p> <p>21 it's -- it's obviously disputable, at the very</p> <p>22 least, but there's no citation, so it's hard to</p> <p>23 know how to -- how to process this.</p> <p>24 BY MS. PARFITT:</p> <p>25 Q If this is the FDA's position with</p>

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 434</p> <p>1 regard to whether or not talc can migrate, do you 2 dispute that? 3 MS. BROWN: Objection. Misstates the 4 document. 5 THE WITNESS: I don't -- I don't dispute 6 that they said it obviously, because it's right 7 here, but there's just no citation for it, and 8 there's no information that tells who in 9 particular thinks that. 10 BY MS. PARFITT: 11 Q Well, the Food and Drug Administration 12 is our regulatory body here in the United States, 13 correct? 14 A It is one. 15 MR. LOCKE: Objection. 16 BY MS. PARFITT: 17 Q All right. Would you agree that 18 dissemination of information that is accurate and 19 truthful is -- is something that they would 20 probably take quite seriously? Would you agree? 21 MS. BROWN: Objection. 22 THE WITNESS: I -- I hope so. 23 BY MS. PARFITT: 24 Q Right. And would you agree that the FDA 25 would not be disseminating information about the</p>	<p style="text-align: right;">Page 436</p> <p>1 think my answer was along the lines of I haven't 2 seen a study that shows that that's true. 3 BY MS. PARFITT: 4 Q We talked about Schildkraut. We talked 5 about Schildkraut, didn't we? 6 A Yeah, they didn't show that either, 7 though. 8 Q When you say they didn't show it, have 9 they opined in medical -- or let me ask you this 10 question. I see the disconnect. 11 Is there evidence contained in 12 peer-reviewed scientific articles wherein it is 13 stated that talcum powder products can migrate to 14 the ovaries? 15 MS. BROWN: Objection. 16 MR. LOCKE: Objection. 17 MS. BROWN: Misstates everything we've 18 looked at and his testimony. 19 THE WITNESS: I think there's been 20 opinions of different people in different articles 21 that are both supportive and not supportive of 22 that statement. 23 BY MS. PARFITT: 24 Q All right. So you've seen scientific 25 writers who have said talc can migrate to the</p>
<p style="text-align: right;">Page 435</p> <p>1 potential for particulates to migrate from the 2 perineum, the vagina to the peritoneal cavity, and 3 say it's indisputable if they didn't have some 4 evidence? 5 MS. BROWN: Objection. Calls for 6 speculation. 7 MR. LOCKE: Objection. 8 THE WITNESS: I don't know why they 9 wrote it. I just think it would be odd to find 10 that the FDA knew this, and it's not out there 11 generally otherwise. I mean I don't -- I don't 12 know what they considered. 13 BY MS. PARFITT: 14 Q When you say it's not out there 15 generally, we talked today about several 16 peer-reviewed articles that have in fact talked 17 about talcum powder part- -- particles migrating 18 to the ovaries, have we not? 19 MS. BROWN: Objection. We have not. 20 THE WITNESS: No, I was going to say, I 21 mean, you've said that a lot, but I mean -- but we 22 haven't looked at a study that shows that. I mean 23 we've talked about whether -- whether or not talc 24 applied to the perineum has been shown to migrate 25 to the ovaries, and a bunch of questions back, I</p>	<p style="text-align: right;">Page 437</p> <p>1 ovaries, and you've seen scientific articles that 2 say that's more questionable. Is that fair? 3 MS. BROWN: Objection. Not fair. 4 Misstates prior -- 5 THE WITNESS: It's sort of fair, but I 6 can't find anybody who's actually shown that it's 7 true. I mean, you know, people may write that, 8 but I mean I haven't seen a study that's shown 9 that you can actually apply talc to the perineum 10 and then find it in the ovaries. 11 BY MS. PARFITT: 12 Q Okay. Let me show you what we'll have 13 marked as exhibit -- oh, thank you. 14 (Counsel conferring.) 15 BY MS. PARFITT: 16 Q It's the end of the day, and we are 17 running out of copies, Doctor. 18 Let me show you -- 19 (Diette Exhibit No. 33 was marked 20 for identification.) 21 MR. ROSEN: Exhibit 33. 22 MS. PARFITT: Beg your pardon? 33? 23 THE WITNESS: This one says 32 on it. 24 MR. ROSEN: Ah, you're correct. 25 BY MS. PARFITT:</p>

Gregory B. Diette, M.D.

Page 438	Page 440
<p>1 Q So I'm going to share this with you, 2 and -- actually, if we could put it on the ELMO, 3 and then I will give it to you so I can at least 4 identify it for counsel. 5 Is that fair? 6 A Yeah. We will see how it goes. 7 Q All right. Let me show you -- it is 8 marked September 30th, 2004, and I will represent 9 that it is to Bill Ashton from Richard Zazenski, 10 and it's a Luzenac document. 11 MS. BROWN: What? I'm going to object 12 on form and foundation. 13 BY MS. PARFITT: 14 Q Okay. Can you see that, Doctor? I 15 don't want to strain your eyes too much. 16 MS. BROWN: No, we need to give him -- 17 he's never seen it. He hasn't reviewed it. His 18 opinions are not based on it. If you want to ask 19 him questions about it, he needs to hold it and 20 look at it. 21 BY MS. PARFITT: 22 Q I'm going to give it to you. I'm going 23 to let you hold it in one moment. 24 Dr. Diette, this is a document I will 25 represent that's dated September 30, 2004, and</p>	<p>1 Take a moment and take a look at that, to eyeball 2 that. 3 MS. BROWN: Take as long as you need to 4 inform your response -- 5 MS. PARFITT: It's a one-page document. 6 MR. LOCKE: No. This -- this is a 7 document that he hasn't seen before. 8 MS. PARFITT: That's correct. 9 MR. LOCKE: Why don't we go off the 10 record. 11 MS. PARFITT: It's one page, Doctor. 12 MS. BROWN: Right, and that's just fair. 13 MS. MILLER: If you're going to ask him 14 questions about what you just threw out there -- 15 MS. BROWN: That's fine. That's fine, 16 but you understand there's no foundation. He's 17 never relied it. 18 MS. PARFITT: Okay, guys -- 19 MS. BROWN: So if we want to ask 20 questions -- 21 THE REPORTER: Excuse me. 22 MS. PARFITT: I'm not having him -- 23 whoa, whoa. 24 (A discussion was held off the record.) 25 BY MS. PARFITT:</p>
Page 439	Page 441
<p>1 that would have preceded any litigation. 2 And it states: "Bill, I came across 3 this paper this morning published in the April 4 2004 journal Human Reproduction, an official 5 journal of the European Society for Human 6 Reproduction and Embryology. It offers some 7 compelling evidence in support of the migration 8 hypothesis. Combine this evidence with the theory 9 that the talc deposition on the ovarian epithelium 10 initiates epithelium inflammation, which leads to 11 epithelium carcinogenesis, and you have a 12 potential formula for NTP classifying talc as a 13 causative agent in ovarian cancer." 14 Now, did I read that correctly? 15 A Yes. 16 Q So let me -- because counsel wants you 17 to hold it, let me have you take -- 18 MS. BROWN: Well, only if you're going 19 to ask him questions about it. 20 MS. PARFITT: I am. I am. But I can't 21 do both. 22 BY MS. PARFITT: 23 Q I've got to hand it to you because she 24 says she wants you to hold it. 25 And attached to that is the article.</p>	<p>1 Q Dr. Diette, I'm simply referring to the 2 cover letter. 3 A Oh. 4 Q And that's all, just one page. Do you 5 see that? 6 A I do. 7 Q Okay. And that's what I just read into 8 the record. Do you see that? 9 A I do. 10 Q Okay. And do you see back in 2004, 11 there was information with regard -- and I have to 12 see it, I can't be -- sorry. I can't memorize it 13 either. 14 So you see back in 2004, the company's 15 being advised that there is indeed literature 16 compelling evidence in support of a migration 17 hypothesis -- 18 MS. BROWN: Object. 19 BY MS. PARFITT: 20 Q -- that was shared between the two 21 companies. 22 Did J&J ever share with you this 23 document that they had in their company files that 24 they had support -- actually compelling evidence 25 of support of the migration hypothesis?</p>

111 (Pages 438 to 441)

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 442</p> <p>1 MS. BROWN: Objection to the speech, 2 lacks foundation. I also believe that's an Imerys 3 document. 4 THE WITNESS: So a few things, right. 5 So one is I -- I've never seen that, so I don't 6 even know what it is. I don't know who those 7 people are. That -- I don't know what their 8 qualifications are to consider something to be 9 compelling evidence or if that's the word that was 10 used. 11 BY MS. PARFITT: 12 Q Mm-hmm. 13 A I have not seen the article that's 14 attached to the back of it. 15 Q Okay. 16 A But it's hard to say much about that. 17 Q Yes. 18 Let me show you what we will have marked 19 as Exhibit 34, and I'll represent to you it's an 20 article by Roberta Ness, "Possible Role of Ovarian 21 Epithelial Inflammation." 22 (Diette Exhibit No. 34 was marked 23 for identification.) 24 BY MS. PARFITT: 25 Q Have you seen this article before?</p>	<p style="text-align: right;">Page 444</p> <p>1 it -- that this -- is this an e-mail or a fax? It 2 has something from Ness's paper or Ness's paper 3 has something from this -- 4 BY MS. PARFITT: 5 Q They have something from Ness's paper, 6 correct. 7 MS. BROWN: Well, objection. 8 THE WITNESS: But this is -- 9 MS. BROWN: Don't -- don't speculate. 10 No one wants you to guess. 11 MS. PARFITT: So we won't talk about -- 12 MS. BROWN: Just wait for a question, 13 and we'll do the best we can. 14 BY MS. PARFITT: 15 Q Okay. Do you see on the first page of 16 Dr. Ness's article, in the left-hand column 17 towards the bottom, where Dr. Ness states: 18 "Inflammation entails cell damage, oxidative 19 stress, and elevations of cytokines and 20 prostaglandins, all of which may be mutagenic. 21 The possibility that inflammation is a 22 pathophysiological contributor to the development 23 of ovarian cancer suggests a directed approach to 24 future research." 25 Do you see that?</p>
<p style="text-align: right;">Page 443</p> <p>1 A I have. 2 Q Okay. Do you see on page 2 -- 3 MS. PARFITT: Where is the other one? 4 (Counsel conferring.) 5 BY MS. PARFITT: 6 Q If I could -- you have in front of you 7 the Zazenski -- thank you. 8 Okay. Now, do you see the graph, I'll 9 call it, it's the chart there on Zazenski? And 10 then look at Figure No. 1. Do you see that, 11 "Inflammation is a common mechanism underlying 12 ovarian cancer"? 13 A I do. 14 Q Okay. And do you see that -- you can 15 look at it. Do you see that that's the same 16 figure in the Zazenski letter as it is in 17 Dr. Ness's letter? Do you see that? 18 MS. BROWN: Objection to the form, lacks 19 foundation. 20 BY MS. PARFITT: 21 Q Or Dr. Ness's report. 22 MS. BROWN: Same objection. 23 THE WITNESS: I mean it -- it looks the 24 same. 25 But what does that mean? Does that mean</p>	<p style="text-align: right;">Page 445</p> <p>1 A I do. 2 Q Okay. Do you agree with that statement? 3 MR. LOCKE: Objection. 4 MS. BROWN: Objection to the form. 5 THE WITNESS: So, I haven't read this 6 article in a while. It is from about 20 years 7 ago. And so I don't know if 20 years ago that was 8 a reasonable thing to consider, but it sounds as 9 if 20 years have gone by and this still hasn't 10 been proven. And so whether I agree with it still 11 now, I'm not sure. I'm not sure if it would be a 12 fruitful endeavor or not. 13 BY MS. PARFITT: 14 Q Does biological plausibility mean that 15 something must be proven? 16 MR. LOCKE: Objection. Asked -- 17 MS. BROWN: Objection. Asked and 18 answered. 19 THE WITNESS: It doesn't mean that 20 it's -- that it's been proven, but it's one of the 21 ways to provide supportive information about 22 whether or not an observed association is causal 23 or not. 24 BY MS. PARFITT: 25 Q Okay. So you agree that you do not --</p>

112 (Pages 442 to 445)

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 446</p> <p>1 one does not need to prove mechanism in order to 2 find causality, correct? 3 A I need to prove -- 4 MR. LOCKE: Objection. 5 MS. BROWN: Objection to form. 6 THE WITNESS: Sorry. Wow, sorry. 7 BY MS. PARFITT: 8 Q We had a chorus. 9 A Yeah. 10 No, you don't need to prove it, but 11 it's -- 12 Q You don't need to prove mechanism. 13 A You don't need to prove mechanism in 14 order to establish causation, but it's hard to get 15 there for a low observed risk if you don't have 16 biological plausibility. 17 Q I'll take that back -- yes, I'm sorry. 18 I hope I didn't ask you this before, but 19 is biological plausibility the same as proof of 20 mechanism? 21 MR. LOCKE: Objection. 22 MS. BROWN: Objection to the form of the 23 question. 24 THE WITNESS: Proof of -- I don't know 25 if I would use the -- so "proof of mechanism"</p>	<p style="text-align: right;">Page 448</p> <p>1 exposure can lead to the outcome that you're 2 interested in. 3 BY MS. PARFITT: 4 Q Okay. Doctor, from your review of the 5 peer-reviewed scientific literature, have you read 6 where study authors who have actually looked at 7 the issue of migration and other biological 8 plausible methods by which talc can get to the 9 ovary? 10 A I guess -- 11 MS. BROWN: I object. I don't 12 understand. 13 THE WITNESS: I mean I've looked at both 14 the human and the animal studies that I could find 15 cited on the topic. And -- and you said that 16 talc -- talc can get to the ovary? 17 BY MS. PARFITT: 18 Q Mm-hmm. 19 A Because, you know, some are not talc, 20 right. There -- there are other kinds of 21 particles or substances. And so I've looked at 22 both the animal and the human studies that I could 23 find. 24 Q And in those studies that you have 25 reviewed, have you seen where those authors who</p>
<p style="text-align: right;">Page 447</p> <p>1 sounds like a term in a way, but maybe not one 2 that's in my vocabulary. Like people talk about 3 proof of concept just as a study design, which -- 4 I don't know if that's the same thing, but I 5 don't -- I don't -- I don't know "proof of 6 mechanism" as a -- as a term. 7 (Counsel conferring.) 8 MS. PARFITT: Let's go off the record 9 for a moment. 10 THE VIDEOGRAPHER: The time is 5:30 p.m. 11 We're going off the record. 12 (Recess.) 13 THE VIDEOGRAPHER: The time is 5:37 p.m. 14 and we're back on the record. 15 BY MS. PARFITT: 16 Q Doctor, what is your definition of 17 "biological plausibility"? 18 MS. BROWN: Objection. Asked and 19 answered. 20 THE WITNESS: I don't have a single one. 21 I think it's in my report somewhere, or at least 22 what I tried to capture from Bradford Hill's 23 statement, but in a general sense, you know, being 24 evidence that whatever -- if we're talking about 25 an exposure, that there is a pathway by which that</p>	<p style="text-align: right;">Page 449</p> <p>1 have studied the issue of biological plausibility 2 and mechanisms by which talc can get to the ovary 3 have concluded in their articles that that is 4 indeed a pathway? 5 MS. BROWN: Objection. 6 MR. LOCKE: Objection. 7 MS. BROWN: Misstates his testimony and 8 the documents. 9 THE WITNESS: That there is -- well, I 10 guess we've got to -- we'd have to look at each 11 one, right. Because, I mean, there's ones like, 12 for example, you know, if we're talking about 13 humans, like where women are basically placed 14 upside down in a -- in an usual position and 15 having something deposited directly into their 16 vagina, and then that may or may not then migrate 17 to their ovaries, but that wouldn't be the same as 18 saying that's a plausible mechanism for applying 19 something to the perineum and then finding it in 20 the ovaries. 21 And then I just want to -- I don't have 22 a lot to say about it, but I would just say with 23 the animals, it looks like certain animals that 24 application of -- of particles does, and then in 25 others it doesn't migrate. And then so I -- I</p>

Gregory B. Diette, M.D.

Page 450	Page 452
<p>1 took that as kind of mixed evidence that even in 2 animals, assuming that there is an appropriate 3 animal model, that they're not getting the same 4 answer based on which animal it is. 5 BY MS. PARFITT: 6 Q Does exposure of a disease have to be 7 proven in order to have a biologically plausible 8 mechanism? 9 MS. BROWN: Objection to the form. 10 MR. LOCKE: Objection. 11 THE WITNESS: So I don't know if I 12 understand that. So are you saying that -- so say 13 it again. I'm sorry. 14 BY MS. PARFITT: 15 Q Sure. It was probably a bad question. 16 MS. BROWN: The realtime -- 17 BY MS. PARFITT: 18 Q Does one need -- does a scientist need 19 to know the precise mechanism in order to 20 determine whether or not it's biologically 21 plausible for some toxin to cause some disease? 22 MS. BROWN: Objection to the form. 23 MR. LOCKE: Objection. 24 THE WITNESS: So "precise" might be a -- 25 a term that matters, but -- but it can be a work</p>	<p>1 MS. BROWN: Objection to the form. 2 MR. LOCKE: Objection. 3 THE WITNESS: So I -- I looked -- for 4 all the things that we talked about -- I don't 5 know which ones we're talking about now in terms 6 of the epidemiology studies. 7 BY MS. PARFITT: 8 Q Correct. 9 A So I've seen some that do and some that 10 don't propose that. Some I think are -- and I'm 11 paraphrasing -- but are sort of more along the 12 lines of we just don't know or there's a lot more 13 work needed, and -- and things of that sort. 14 Q Are there a lot on the lines of 15 migration of talc -- excuse me. 16 Are there a lot of articles that you've 17 reviewed where they have -- authors have stated 18 that talc can migrate to the ovaries? 19 A I wouldn't say -- 20 MS. BROWN: Objection. 21 THE WITNESS: I wouldn't say a lot. And 22 I haven't seen anything as strong as that FDA 23 statement, you know, I mean, where -- where 24 there's some, you know, certainty that is coupled 25 with that kind of a statement.</p>
Page 451	Page 453
<p>1 in progress in the sense that you can have some 2 information or no information or lots of 3 information. So there can be, you know, quite a 4 spectrum of information you would have about the 5 plausibility. 6 BY MS. PARFITT: 7 Q I think what I'm asking is, does the 8 mechanism of disease need to be proven in order to 9 find causality? 10 MS. BROWN: Objection to the form. 11 THE WITNESS: I -- I think we keep doing 12 this over and over, because this -- I think -- I 13 think this is the same -- unless it's meant to be 14 different, like I don't know how to answer that 15 differently. It's -- you know, obviously it 16 doesn't have to be proven, but it certainly is 17 important. And when you have a very small 18 estimated risk, then it becomes even more 19 important. 20 BY MS. PARFITT: 21 Q Okay. Have you seen in the literature 22 that you've reviewed numerous authors who have 23 proposed a biologically plausible mechanism by 24 which talcum powder products can cause ovarian 25 cancer?</p>	<p>1 BY MS. PARFITT: 2 Q But you've certainly seen where the 3 authors have opined and discussed biologically 4 plausible mechanism by -- mechanisms by which 5 talcum powder products can cause ovarian cancer. 6 MR. LOCKE: Objection. 7 MS. BROWN: Objection. Continues to 8 misstate his testimony. 9 THE WITNESS: What's -- what's different 10 about that than what I already answered? 11 BY MS. PARFITT: 12 Q Well, what I'm trying to get at is, 13 whether or not you believe it or don't believe it, 14 I'm simply trying to understand from you whether 15 or not in your read of the scientific literature 16 have you seen where authors who have actually 17 studied this topic where they have determined and 18 written in their reports that there are 19 biologically plausible mechanisms by which talc 20 can migrate to the ovaries? 21 MR. LOCKE: Objection. 22 MS. BROWN: No, objection. He's 23 answered this a hundred times, and it's -- 24 BY MS. PARFITT: 25 Q And if it's no, then it's no. If you've</p>

114 (Pages 450 to 453)

Gregory B. Diette, M.D.

Page 454	Page 456
<p>1 seen it, you've seen it. If you dispute it, you</p> <p>2 dispute it.</p> <p>3 A Well, it's -- it's none of those.</p> <p>4 But you just said reports. Does that --</p> <p>5 are we now talking about expert reports or are --</p> <p>6 Q No.</p> <p>7 A -- we still talking about --</p> <p>8 Q No, we're still talking --</p> <p>9 A Okay. We're talking about like</p> <p>10 peer-reviewed publications?</p> <p>11 Q That's right.</p> <p>12 A So I've seen a mixture, yeah. It's like</p> <p>13 when you look at the epi literature, I mean the --</p> <p>14 the way I read it is like -- is, you know, an</p> <p>15 epidemiologist is supposed to be able to get up to</p> <p>16 speed without becoming an expert in absolutely</p> <p>17 everything, right?</p> <p>18 So I already told you I'm not a cancer</p> <p>19 biologist, but I do count on the authors to set</p> <p>20 the stage with the introduction and then interpret</p> <p>21 their findings and the discussion and sort of take</p> <p>22 us at least partway towards there.</p> <p>23 So even the recent meta-analysis, if you</p> <p>24 look at Berge or Burge (phonetic), however you say</p> <p>25 that, and Penninkilampi, you know, they talk about</p>	<p>1 probably means one thing in the world in general.</p> <p>2 I think if you're talking about Rothman, yeah,</p> <p>3 Rothman has written about that --</p> <p>4 BY MS. PARFITT:</p> <p>5 Q Right.</p> <p>6 A -- and about it being simply a</p> <p>7 competition of sort of counting those that are</p> <p>8 significant and those that are not.</p> <p>9 I didn't see that. I think the way I</p> <p>10 described it I think was -- was the way I</p> <p>11 approached it, which said some of the information</p> <p>12 that's available is that some of the studies were</p> <p>13 statistically significant and some weren't. It's</p> <p>14 informative, but it's not literally the same as</p> <p>15 saying, I'm just going to count them up and stop</p> <p>16 there.</p> <p>17 Q Because that would be improper, correct?</p> <p>18 MS. BROWN: Objection.</p> <p>19 THE WITNESS: To only do that, yes.</p> <p>20 BY MS. PARFITT:</p> <p>21 Q Okay. All right. Let me ask a couple</p> <p>22 of question -- questions.</p> <p>23 What is the minimal level of exposure to</p> <p>24 cigarette smoke in terms of cigarette smoke at</p> <p>25 home that's necessary to cause lung cancer?</p>
Page 455	Page 457
<p>1 there -- there being uncertainty about the</p> <p>2 mechanism. So I'm just saying even as recently as</p> <p>3 the -- the very latest meta-analysis, there's</p> <p>4 uncertainty expressed.</p> <p>5 Q Do you see uncertainty being expressed</p> <p>6 by biologically plausible mechanisms?</p> <p>7 MS. BROWN: Objection.</p> <p>8 THE WITNESS: Well, I don't know if</p> <p>9 they're plausible or not. I mean that's the whole</p> <p>10 point, right? You know, I mean you can say</p> <p>11 something, but it doesn't make it true.</p> <p>12 BY MS. PARFITT:</p> <p>13 Q You reminded me of something. In your</p> <p>14 review of the various case-control studies, did</p> <p>15 you exercise a process known as vote counting?</p> <p>16 MS. BROWN: Objection.</p> <p>17 THE WITNESS: No.</p> <p>18 BY MS. PARFITT:</p> <p>19 Q You did not?</p> <p>20 A I did not.</p> <p>21 Q That would be improper to do so,</p> <p>22 correct?</p> <p>23 MS. BROWN: Objection.</p> <p>24 THE WITNESS: Well, if we're talking --</p> <p>25 so I guess, just to be clear, so vote counting</p>	<p>1 MS. BROWN: Form.</p> <p>2 THE WITNESS: I do not know.</p> <p>3 BY MS. PARFITT:</p> <p>4 Q Okay. What is the minimal level of</p> <p>5 exposure to asbestos fibers inhaled that is</p> <p>6 sufficient to cause ovarian cancer?</p> <p>7 MS. BROWN: Form.</p> <p>8 MR. LOCKE: Objection.</p> <p>9 THE WITNESS: We -- we did that before.</p> <p>10 I don't -- I don't have any more information than</p> <p>11 what I did, like meaning, you know, I have some --</p> <p>12 some guideposts like the -- the Whitnum 40</p> <p>13 fiber/cc years of -- of crocidolite, which did not</p> <p>14 seem to be adequate to cause it.</p> <p>15 And then, you know, when we looked at</p> <p>16 the IARC, I didn't -- even when you and I looked</p> <p>17 at it together, I didn't see information that</p> <p>18 talked about what dose would be required.</p> <p>19 BY MS. PARFITT:</p> <p>20 Q Okay. Same question. What's the</p> <p>21 minimal level of exposure to asbestos fibers</p> <p>22 inhaled that is sufficient to cause mesothelioma?</p> <p>23 MS. BROWN: Objection.</p> <p>24 MR. LOCKE: Objection.</p> <p>25 THE WITNESS: Pleural or peritoneal</p>

115 (Pages 454 to 457)

Gregory B. Diette, M.D.

Page 458	Page 460
<p>1 or --</p> <p>2 BY MS. PARFITT:</p> <p>3 Q Pleural.</p> <p>4 A So the -- so the amount for pleural</p> <p>5 mesothelioma is -- and did you say fiber type or</p> <p>6 you didn't mention fiber type?</p> <p>7 Q I didn't. I just said fibers.</p> <p>8 A Okay. So it would matter fiber type.</p> <p>9 If it's chrysotile predominant, then above 200 to</p> <p>10 400 fiber/cc years would be, you know, one</p> <p>11 estimate of the dose. If it's crocidolite, you</p> <p>12 know, you could divide that by 500. And if it's</p> <p>13 amosite, by a hundred, and other amphiboles, you</p> <p>14 know, somewhere in between those sort of ranges.</p> <p>15 And so, you know, I think for</p> <p>16 amphiboles, above like the single digit fiber/cc</p> <p>17 years, and for chrysotile, above the couple of</p> <p>18 like 200 to 400 fiber/cc years.</p> <p>19 Q Is it true that the dose-response curve</p> <p>20 for any genotoxic carcinogen intersects with zero?</p> <p>21 MS. BROWN: Objection to the form.</p> <p>22 THE WITNESS: Well, there's got to be a</p> <p>23 zero point if there's zero exposure, right? If</p> <p>24 there's literally zero exposure, then there can't</p> <p>25 be -- there can't be a signal from that zero.</p>	<p>1 Q Okay. You criticize the plaintiffs'</p> <p>2 experts for what you called a muted examination of</p> <p>3 the case-control studies that they reviewed.</p> <p>4 Do you remember saying that in your</p> <p>5 report?</p> <p>6 A I don't remember that word, but it's --</p> <p>7 it makes a lot of sense to me.</p> <p>8 Q Okay. Where in your port -- report did</p> <p>9 you set forth all of the limitations and</p> <p>10 weaknesses of the cohort studies of talcum --</p> <p>11 talcum powder products and asbestos -- and ovarian</p> <p>12 cancer?</p> <p>13 A Well, there's a bunch, right. So --</p> <p>14 Q Well, where did you --</p> <p>15 A I'm telling you.</p> <p>16 Q -- provide us in your report that</p> <p>17 information --</p> <p>18 A I'm telling you.</p> <p>19 MS. BROWN: Let him finish --</p> <p>20 THE WITNESS: I understand your</p> <p>21 question.</p> <p>22 MS. BROWN: -- and answer your question.</p> <p>23 THE WITNESS: So one of the criticisms,</p> <p>24 which I think is pretty profound, which is the</p> <p>25 lack of a validated measure of talcum powder</p>
Page 459	Page 461
<p>1 BY MS. PARFITT:</p> <p>2 Q What does the -- what does it mean if a</p> <p>3 dose-response curve intersects zero?</p> <p>4 MS. BROWN: Form.</p> <p>5 BY MS. PARFITT:</p> <p>6 Q What does that mean?</p> <p>7 A It's not a term that's familiar. I</p> <p>8 mean, it's just -- I'm not sure -- if you've got</p> <p>9 zero exposure, you can't have any outcome from</p> <p>10 that. So I -- I assume that's what we're talking</p> <p>11 about is just like a -- like a no exposure</p> <p>12 estimate.</p> <p>13 If you're talking about like -- the</p> <p>14 place I've seen people talk about it is like with</p> <p>15 low doses of things and what happens, you know,</p> <p>16 below the concentration or the level at which</p> <p>17 there's known effects, then what happens between</p> <p>18 there and zero. But if it's literally zero -- if</p> <p>19 there's literally zero exposure, it's got to be</p> <p>20 zero outcome.</p> <p>21 (Counsel conferring.)</p> <p>22 BY MS. PARFITT:</p> <p>23 Q Okay. You reviewed the cohort studies</p> <p>24 in this case, correct?</p> <p>25 A The three -- three cohort studies.</p>	<p>1 exposure that could have someone estimate whether</p> <p>2 or not somebody is exposed at all or whether or</p> <p>3 not there's a dose-response, and that applies to</p> <p>4 all the studies, right. So that's uniformly</p> <p>5 applied to whether they're case-control studies</p> <p>6 or -- or cohort studies.</p> <p>7 BY MS. PARFITT:</p> <p>8 Q That would be the exposure</p> <p>9 misclassification.</p> <p>10 MS. BROWN: Objection.</p> <p>11 THE WITNESS: No, no, no. So it would</p> <p>12 be -- you could misclassify it, but it -- but what</p> <p>13 I'm talking about is, that in order to measure an</p> <p>14 exposure, you need a valid measure of that</p> <p>15 exposure. That doesn't exist, or at least if it</p> <p>16 exists, it hasn't been employed in the -- in the</p> <p>17 published literature. And that applies to the</p> <p>18 cohort studies and the case controls.</p> <p>19 What I -- what I did was I tried to</p> <p>20 actually not denigrate any of the study designs.</p> <p>21 I thought that was appalling. You know, when you</p> <p>22 talk about where this came from, you know, to sort</p> <p>23 of single out the cohort studies repeatedly by</p> <p>24 the -- by the plaintiffs' expert and say, you</p> <p>25 know, This is a terrible design, or this is</p>

116 (Pages 458 to 461)

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 462</p> <p>1 terrible for whatever reason, it's extraordinary, 2 and it's -- to me it's unprecedented for -- for 3 epidemiologists or other healthcare professionals 4 to sort of look at cohort studies and find that 5 those are so awful, and that case-control studies 6 are suddenly so sturdy. It doesn't make any 7 sense. 8 So -- so for me, like the task wasn't 9 really so much -- I wasn't trying to criticize 10 either form of the study, but just to point out 11 realistically that there are biases, that there 12 are confounding issues, and -- and things of 13 that -- that sort. 14 BY MS. PARFITT: 15 Q In your review of the literature for 16 purposes of your opinions today, did you see 17 evidence from any of the studies that you read 18 that there was a dose-response associated between 19 talcum powder products and ovarian cancer? 20 A So in total, no. In a couple of 21 studies, there are purported dose-response 22 findings, right. So the latest Cramer study is an 23 example. There may have been another, but there 24 are so many studies that show absolutely the 25 opposite, meaning either flat dose-response,</p>	<p style="text-align: right;">Page 464</p> <p>1 Q Okay. So you would agree with me there 2 are studies in the peer-reviewed literature that 3 have demonstrated a dose-response between talcum 4 powder products and ovarian cancer? 5 MS. BROWN: Objection -- 6 MR. LOCKE: Objection. 7 MS. BROWN: -- to the form. 8 MS. PARFITT: Let him answer, please. 9 MS. BROWN: I get to object. 10 THE WITNESS: I think just a couple. 11 MS. PARFITT: Let's go off the record. 12 THE VIDEOGRAPHER: The time is 5:53 p.m. 13 We're going off the record. 14 (Recess.) 15 THE VIDEOGRAPHER: The time is 5:58 p.m. 16 We're back on the record. 17 MR. HEASLIP: Can we go off for one 18 moment? I apologize. 19 THE VIDEOGRAPHER: The time is 5:58 p.m. 20 We're going back off the record. 21 (A discussion was held off the record.) 22 THE VIDEOGRAPHER: The time is 5:59 p.m. 23 We're back on the record. 24 CROSS-EXAMINATION 25 BY MR. FINCH:</p>
<p style="text-align: right;">Page 463</p> <p>1 upside down dose-response, zig-zaggy, haphazard 2 dose-response. So I would say looking at the 3 evidence in total, it's a mess. I mean it's 4 certainly not supportive. 5 And I'll you the truth, if you go back 6 to -- like to 2000 -- and I know we're in a hurry, 7 so I will try to talk a little faster -- but the 8 Rothman -- the Rothman review, at least up until 9 2000, they -- they plotted out all the 10 dose-response they found, and they found an 11 inverse relationship overall, which is one of the 12 things they found to be inconsistent with there 13 being causation. 14 So I think, you know, from 1982, when 15 the first case-control study was published, to 16 2000, at least when it's assessed by Rothman and 17 his colleagues, is actually upside down. 18 Q What about Terry? Terry in 2013 19 reported a dose-response, did they not? 20 MS. BROWN: Objection to the form. 21 THE WITNESS: I don't remember what they 22 showed. I don't -- I don't doubt you, but I -- 23 but there's just -- there's a couple of studies 24 that have demonstrated that. 25 BY MS. PARFITT:</p>	<p style="text-align: right;">Page 465</p> <p>1 Q Good afternoon, Dr. Diette. My name is 2 Nate Finch. You and I have met before, correct? 3 A Yes. 4 Q You were asked a question about the 5 dose-response curve to genotoxic carcinogens. Do 6 you recall that question? 7 A I do. 8 Q And your answer was something to the 9 effect of if the dose was zero, then it would be 10 an intersection of zero. 11 Do you recall that answer? 12 A Something like that. 13 Q All right. I want you to assume that 14 we're talking about a dose-response curve where 15 there is a positive dose, not a dose of zero. 16 Your typical dose-response curve looks something 17 like this (indicating), right, with dose on the 18 X-axis and response on the Y-axis? 19 A You can draw it that way. 20 MS. MILLER: Is that a exhibit? 21 MR. FINCH: You can mark it as an 22 exhibit. It's got somebody's notes on the back of 23 it, but... 24 BY MR. FINCH: 25 Q Isn't it true, Dr. Diette, that for a</p>

Gregory B. Diette, M.D.

Page 466	Page 468
<p>1 genotoxic carcinogen where there is a positive 2 dose, the dose-response curve always intersects 3 with zero? 4 MS. BROWN: Objection to form. 5 THE WITNESS: That's not something that 6 I say. I mean I don't -- people may say that, but 7 I -- I think when we're talking about -- like zero 8 is zero, right. So zero exposure means zero risk. 9 BY MR. FINCH: 10 Q I'm not -- I'm not talking about zero. 11 MS. BROWN: Wait, let him finish, 12 please. 13 THE WITNESS: Well, I know. That's what 14 I'm talking about when I -- when I hear that 15 question. 16 BY MR. FINCH: 17 Q All right. So if someone were to 18 testify when you're talking about a genotoxic 19 carcinogen where there is a positive exposure, 20 there -- the dose-response curve intersects with 21 zero, meaning that there -- isn't it true that 22 that means that there -- at any level of exposure, 23 there's an excess risk of cancer for a genotoxic 24 carcinogen? 25 MS. BROWN: Objection to the form.</p>	<p>1 about the sort of mechanical process of writing 2 your report. Do you remember that? 3 A I do. 4 Q And to be clear, Doctor, did you write 5 every substantive word of the expert report that 6 we've marked as an exhibit in this case? 7 A To the -- yes, everything substantive. 8 Q Did MSA or Medical Science Affiliates 9 make any substantive contributions to your expert 10 report in this proceeding? 11 A No. 12 Q You spoke a little bit earlier today 13 about some administrative support that you 14 received from MSA. Do you remember that? 15 A I do. 16 Q And tell us what you meant by 17 "administrative support." 18 A So by "administrative support," I meant, 19 you know, gathering -- like collating materials 20 for me, helping to -- to format the report, you 21 know, putting -- you know, putting the reference 22 citations in correctly. You know, creating the -- 23 the list of reliance documents at the end. You 24 know, things of that sort. And then -- and then 25 generating invoices.</p>
Page 467	Page 469
<p>1 THE WITNESS: So I don't know. That may 2 be part of some field that's not my field. But I 3 -- but in the fields that I work in, I recognize 4 that you need a certain amount of exposure in 5 order to cause a disease, including cancer. 6 BY MR. FINCH: 7 Q Okay. But you cannot dispute that 8 genotoxic carcinogens, the dose-response curve 9 intersects with zero. You haven't studied that 10 issue; is that correct? 11 MR. LOCKE: Objection. 12 MS. BROWN: Objection to the form. 13 THE VIDEOGRAPHER: Seven hours. 14 MS. BROWN: You're done. Wait. 15 THE WITNESS: So I mean, my answer is 16 the same as it was before. 17 MS. BROWN: I can ask from here. 18 (A discussion was held off the record.) 19 CROSS-EXAMINATION 20 BY MS. BROWN: 21 Q Good evening, Dr. Diette. 22 A Hi. 23 Q Just a couple of quick questions, and we 24 will get you on your way. 25 We had some discussion earlier today</p>	<p>1 I'm trying to think what else. 2 Whatever -- whatever I said earlier was the -- was 3 the full list, I think. 4 Q You also mentioned earlier today 5 receiving some editorial support from the folks at 6 MSA. Tell us what you meant by that. 7 A So to look for typos or -- I gave the 8 example of like where I had a really long 9 paragraph, and they broke it up with bullets to 10 make it look more readable, that sort of thing, 11 and -- and just making this actually have the 12 physical appearance that it does. 13 Q Did MSA provide anything other than 14 administrative formatting type support in 15 connection with your report in this case? 16 A No. 17 Q If someone were to suggest that the 18 opinions in your expert report are not entirely 19 your own, would that be the truth? 20 A I'm sorry. I was reading that going by, 21 and I didn't listen. 22 Q Sure. If someone were to suggest that 23 some of the opinions in your expert report are not 24 entirely your own, would that be the truth? 25 A No.</p>

118 (Pages 466 to 469)

Gregory B. Diette, M.D.

<p style="text-align: right;">Page 470</p> <p>1 MS. PARFITT: Objection. 2 THE WITNESS: They're -- they're all my 3 opinions. 4 BY MS. BROWN: 5 Q If someone were to suggest that MSA 6 wrote some of the substantive pieces of your 7 report, would that be the truth? 8 MS. PARFITT: Objection. 9 THE WITNESS: No. 10 MS. BROWN: Thanks very much for your 11 time, Dr. Diette. I have no further questions. 12 MS. PARFITT: Anybody? No. Thank you. 13 Dr. Diette, thank you very much. 14 THE WITNESS: Thank you. 15 MS. PARFITT: I appreciate it. 16 THE VIDEOGRAPHER: The time is 6:04 17 p m., April 9th, 2019. Going off the record, 18 completing the videotaped deposition. 19 (Whereupon, the deposition of 20 GREGORY B. DIETTE, M.D. was 21 concluded at 6:04 p m.) 22 23 24 25</p>	<p style="text-align: right;">Page 472</p> <p>1 INSTRUCTIONS TO WITNESS 2 Please read your deposition over carefully and 3 make any necessary corrections. You should state 4 the reason in the appropriate space on the errata 5 sheet for any corrections that are made. 6 After doing so, please sign the errata sheet 7 and date it. 8 You are signing same subject to the changes 9 you have noted on the errata sheet, which will be 10 attached to your deposition. It is imperative 11 that you return the original errata sheet to the 12 deposing attorney within thirty (30) days of 13 receipt of the deposition transcript by you. If 14 you fail to do so, the deposition transcript may 15 be deemed to be accurate and may be used in court. 16 17 18 19 20 21 22 23 24 25</p>
<p style="text-align: right;">Page 471</p> <p>1 CERTIFICATE OF CERTIFIED SHORTHAND REPORTER 2 The undersigned Certified Shorthand Reporter 3 does hereby certify: 4 That the foregoing proceeding was taken before 5 me at the time and place therein set forth, at 6 which time the witness was duly sworn; That the 7 testimony of the witness and all objections made 8 at the time of the examination were recorded 9 stenographically by me and were thereafter 10 transcribed, said transcript being a true and 11 correct copy of my shorthand notes thereof; That 12 the dismantling of the original transcript will 13 void the reporter's certificate 14 In witness thereof, I have subscribed my name 15 this date: April 10, 2019 16 17 _____ 18 LESLIE A TODD, CSR, RPR 19 Certificate No 5129 20 (The foregoing certification of 21 this transcript does not apply to any 22 reproduction of the same by any means, 23 unless under the direct control and/or 24 supervision of the certifying reporter) 25</p>	<p style="text-align: right;">Page 473</p> <p>1 ----- 2 E R R A T A 3 ----- 4 PAGE LINE CHANGE 5 _____ 6 REASON: _____ 7 _____ 8 REASON: _____ 9 _____ 10 REASON: _____ 11 _____ 12 REASON: _____ 13 _____ 14 REASON: _____ 15 _____ 16 REASON: _____ 17 _____ 18 REASON: _____ 19 _____ 20 REASON: _____ 21 _____ 22 REASON: _____ 23 _____ 24 REASON: _____ 25</p>

119 (Pages 470 to 473)

Gregory B. Diette, M.D.

Page 474

ACKNOWLEDGMENT OF DEPONENT

I, _____, do hereby
certify that I have read the foregoing pages, and
that the same is a correct transcription of the
answers given by me to the questions therein
propounded, except for the corrections or changes
in form or substance, if any, noted in the
attached Errata Sheet.

GREGORY B. DIETTE, M.D. DATE

Subscribed and sworn to
before me this
____ day of _____, 20____.
My commission expires: _____

Notary Public

A	accessory 75:25 76:13	administer 13:20	162:19 163:22 164:10 165:6	278:9 282:19 283:6 287:2
a.m 1:18 13:7 19:13 44:15,18 89:7 151:17,20	accompany 159:19	administering 2:18	165:21 166:25 168:3,18	291:11 292:24 302:17 304:2
AACES 11:11	account 77:1 255:8 383:20	Administration 228:1 434:11	170:24 179:7 179:14 188:21	304:20,23 306:5 321:5,13
abandon 309:24 312:8	accounts 36:6 36:14	administrative 91:17 93:9 154:19 158:6	189:7 190:16 190:19,20 468:8	321:16 322:16 322:22 331:3 361:22 362:6
abandoning 201:13 306:24 309:5	accurate 14:24 100:1 139:12 387:14,16 434:18 472:15	178:17 183:2,6 468:13,17,18 469:14	Affiliates' 155:18 156:5	362:21 363:10 367:22,25
abide 38:24	accurately 73:19 97:20 274:19	admonishing 38:6,7 113:10	Affiliations 7:15	368:14 400:4
ability 378:21	acknowledged 182:7	adult 403:22	affirmative 415:13	401:21 411:8 413:7 414:24
able 36:17 69:9 85:16 140:19 158:1 207:21 216:13 300:17 319:14 372:8 391:1 410:12 454:15	ACKNOWLEDGE... 474:1	adults 374:20 389:19	afforded 179:14	416:3 417:23 418:1,2,3
abnormality 372:20	active 408:16	advance 88:17	afield 270:12	420:8 432:12
absolute 361:9	activities 10:14 205:8	advanced 45:20 45:25	afternoon 204:25 205:1 465:1	433:12 434:17 434:20,24 445:2,10,25 464:1
absolutely 62:13 65:23 84:8 86:22 387:14 387:16 415:14 454:16 462:24	actual 172:4 203:21 264:19	advertise 189:4 188:21	age 249:15	agreeable 46:24 293:4 303:21 305:3 306:11 319:9
absorbed 405:17	ADAM 3:5	advertisement 188:15	agent 285:20 439:13	agreement 31:21 32:6 33:18 153:22 154:4 187:11
absorption 266:21	add 24:21 91:25 96:16 97:7 178:1,19 179:22 234:20	advised 441:15	ago 51:2 108:17 117:10 152:20 153:10 189:18 231:1 244:17 418:4,9 445:7 445:7	agreements 33:2 156:8
abstract 282:9 365:2,10 366:18 369:22 428:5	added 347:5	affidavit 133:12 135:14 197:12 197:25 198:19	agree 34:23 35:3 45:24 46:20 47:12 84:6,9 84:20 87:16,21 88:8 107:23 112:21 183:5 213:2 216:4,4 216:13,24,25 217:8,14,15 219:21 222:1,6 225:25 226:3,9 226:15 233:25 235:3 236:23 260:3,3,8 272:13 274:25 275:24 276:18 276:19,21,25 277:1,2,2,12	Ah 437:24 ahead 16:6 23:22 24:17 25:22 26:20,21 58:7 63:1 162:8,9 192:22 212:8 216:2 218:14 270:5 275:6 292:10 297:12 304:11 353:22,23 355:2,11 365:18
Abstracts 8:12	adding 40:4	affidavits 130:7 131:2,14 134:14 135:1 170:18 196:25 197:6 198:18		air 102:13 107:21 371:17 373:21 405:20
absurd 270:15 271:2	addition 134:13 183:10 211:19	affiliate 187:19 187:23		
academic 93:18 149:11	additional 25:16 29:11 31:12 92:13 178:10	affiliated 155:15		
accepted 92:1 368:3	additions 91:23 139:15	Affiliates 24:20 25:18 31:18,21 31:25 32:7 33:4,5,20 151:23 152:6 152:10,18,23 153:15 154:8 155:10,16 157:4,8 158:10 159:8,21 162:5		
accepts 291:9 292:20	address 31:2 124:21 142:11 142:15,19			
access 10:13 26:15 285:17	addressing 134:15			
	adequacy 57:1			
	adequate 457:14			
	adhere 317:2			
	adjusted 249:22			

airborne 373:14 373:15 406:7	amphiboles 458:13,16	122:3 124:2	220:9,18 224:3	296:23 297:22
airway 97:16 101:9	Amrhein 9:5,14	125:1 135:23	228:21 232:7	305:10
al 9:14 271:17	analogous 371:11	136:13 137:10	251:6 261:17	appears 26:3
alert 47:19	analyses 77:12	139:25 140:24	308:3 385:5	123:24 282:14
Ali 19:15 27:9	336:8,15	141:18 144:5	423:1 429:10	407:5,19
all-cause 10:9	analysis 76:1,15	146:17 150:25	445:18 447:19	appendices 265:10
366:3 367:3	145:23 148:22	156:15 159:4	453:10,23	Appendix 7:8,19
389:18	149:5 251:12	161:10 164:13	answering 33:9	66:4 121:4
allegation	252:16,24,25	164:15 165:13	61:19 203:4	application
109:21	267:24 268:15	166:20 167:6	244:12 335:19	266:22 270:25
allegations	268:23 269:16	168:13 169:8	337:19 404:14	332:21,25
109:2,15,25	270:14 271:1,4	173:22 176:16	answers 14:23	416:8 449:24
110:10	333:8,9 334:19	176:17,19	37:13 106:24	applications 420:22,25
Allen 309:7	335:22,24	177:2,10	193:2 474:5	applied 149:13
allergen's	336:10,17	187:13 191:22	anybody 15:12	250:18 412:23
107:25	338:21 339:21	191:23 192:21	56:24 153:6	435:24 461:5
allergens 102:15	342:14 361:3	195:6 198:8	164:19 192:19	applies 461:3,17
102:19,23	analyzing 425:4	207:22 210:9	196:11 266:10	apply 74:7 401:2
103:7 107:22	and/or 135:13	218:8 220:10	266:13 311:22	437:9 471:21
ALLISON 4:17	471:23	249:18 268:19	313:24 340:12	applying 362:13
allowed 62:11	angles 200:25	274:18,20,23	437:6 470:12	449:18
166:5	animal 252:6	274:24 276:6	anymore 29:24	appointment
Almighty 231:10	253:3 285:8	276:10,10	30:17 153:1	93:19 97:1,3
alter 76:1,14	448:14,22	288:4,4 304:5	294:23	100:20
ambient 370:18	450:3,4	310:22 319:22	anyway 49:8	appreciate
371:17	animals 254:7	326:13 332:4	79:4 305:1	40:11 67:24
America 11:24	254:12 449:23	336:3 337:22	317:6 372:6	88:25 114:10
49:20	449:23 450:2	338:3,10	apart 18:16	114:11 140:13
American 9:9	Ann 235:22	346:22 371:3	apologize 66:1	183:10 184:3
11:10 94:20	Anne 2:16 8:5	372:6,8 374:13	202:17 284:22	190:13 251:1
239:4 295:6,18	annoy 53:9	407:1 419:11	312:12 378:3	327:7 345:3,15
296:24 298:12	327:4	421:2 424:20	378:16 394:17	349:6 355:12
301:2 308:17	answer 23:22	424:23,25	426:21,23	381:13 400:10
308:19 309:4	24:11 26:24	436:1 450:4	464:18	411:7 470:15
387:7	29:6 32:22	451:14 460:22	appalling	approach
amosite 458:13	33:15,18,21	464:8 465:8,11	461:21	146:20 241:5
amount 23:14	35:17 37:18,23	467:15	apparently	245:12 250:23
23:15 40:8	41:17 55:21	answerable	257:14 312:12	319:25 343:7
90:7,19 176:4	62:12,18,23	90:11	391:10	343:14 444:23
178:19 179:23	67:11 68:6,7	answered 35:8	appear 31:15	approached
180:1 280:25	73:12,15 78:24	57:14 68:12	147:7 172:4	456:11
383:13 458:4	79:7 80:20	74:25 117:21	232:1 313:4	appropriate
467:4	82:18 83:18	127:22 146:13	appearance	39:9 173:22
amounts 282:15	84:8,13 93:16	147:24 150:15	469:12	253:25 339:14
285:25	106:11 117:22	161:10 184:12	appearances 4:1	450:2 472:4
		210:8 217:21	5:1 13:18	
		218:7 219:1	appeared	

appropriately 287:16	258:21 280:17 281:23 282:6	78:17 79:18,25 79:25 80:9	122:6 186:19 387:11 388:6	57:1,2 59:16 64:16 68:17
approximately 36:20,22 45:21 46:2 121:10,15 213:25	296:9 297:22 297:24 298:6 304:5 305:9 306:17 309:4	84:6,11,17,22 87:18,25 89:14 89:17,21 90:13 90:18,19	asbestos/meso- 207:10 asbestosis 122:10	77:19 83:16 109:10 132:20 135:21 136:11 136:15 146:6
April 1:17 11:22 13:6 121:15 175:9 229:10 439:3 470:17 471:15	309:15,22 317:16,21 328:5 336:22 343:20 369:9 373:25 419:14 424:16,19	120:16 121:21 122:5,21,24 123:7,14,22,24 125:22,24 126:5,20 127:5 127:20,25 128:14,20	ascend 417:17 418:5 ascertain 406:18 ASHCRAFT 3:6	148:23 163:10 164:15 191:5 192:24 193:3 195:16 201:1 205:23 221:4
arbitrary 251:19 302:14	426:3 427:9,21 428:1 439:25 442:13,20,25 444:16 445:6	136:16,19,23 142:20 147:17 148:13 187:15 201:24 203:16 214:20 215:7 215:10 225:24 226:8,14 241:2 241:4,9 259:23 259:24 261:23 262:10 263:11 281:6,13,24 282:12,13 283:9,19 284:8 284:9,13 285:12,22,25 286:9 382:13 383:2,10,14 384:5,14,17 385:13,21 386:10 387:6 387:10 388:12 388:25 389:4 389:20 391:2 391:17,22 392:7 394:1,24 395:2 397:17 399:14,17,17 400:20 401:2 401:21,22,25 402:7 457:5,21 460:11	Ashton 11:25 438:9 aside 44:3 134:25 206:4 208:23 231:10 285:23 286:15 asked 19:21 20:20 21:11 23:24 27:22,23 32:13 35:7 49:23,25 55:21 55:25 57:10,17 57:21 74:24 106:11,13 112:17 117:21 127:21 147:23 148:1 150:15 155:6 181:16 181:25 184:20 184:21 185:7 187:2 193:12 195:9 196:16 199:13 200:5 200:14 210:9 218:7 220:18 224:2 228:21 232:7 251:5 261:17 262:6 262:10 275:18 276:9 308:3 377:24 422:25 429:10 445:16 445:17 447:18 465:4 asking 37:12 42:11 53:2	235:10 238:14 246:13 252:11 263:6 299:1 304:16 329:14 336:15 337:10 400:4 403:10 404:14 409:16 422:7 430:24 451:7 aspect 355:25 356:2 aspects 256:24 aspirin 421:17 421:20,21 assemble 244:20 assert 33:12 asserted 33:9 asserting 33:13 33:15 assess 266:20 assessed 463:16 assessing 239:10 assessment 8:11 11:18 144:8 256:9 264:23 265:3,19 267:6 268:11 272:17 273:20,24 274:12 275:25 277:22 427:11 assistance 159:18 178:11 179:7 250:11 assistant 93:10 250:15 assistants 91:17
area 51:17 59:4 75:7 128:20 151:15 184:10 190:17 203:1 214:24 216:21 217:10 218:3 219:8 220:12 221:6 236:15 237:16 260:23 276:1 279:2 280:4 288:8 331:14 430:3	articles 28:2,9 28:11,13,13,17 28:18,18 29:7 30:5,7,10 31:4 31:11 37:11 92:13,16 122:13 149:9 240:15,21 299:5,11 309:10,11 310:14 347:13 364:21 425:24 433:18 435:16 436:12,20 437:1 449:3 452:16 articulate 145:21 articulating 88:11 288:12 asbestiform 72:17,21 73:5 73:23,24 74:5 401:4,9 asbestos 8:16 11:5 41:14,20 64:25 72:6,23 73:20,21 74:1 74:8 75:24 76:12 77:1,16 77:22 78:4,11	asbestos- 121:21 123:22 asbestos-related		
areas 19:3 80:15 100:22 203:14 356:18 Armhein 317:25 ARPS 5:10 arrange 162:15 arrangement 154:7 arranging 162:13 arrive 222:23 arrived 105:7 Arsenic 10:23 393:16 article 6:23 8:16 8:22 9:4,7 10:4 10:9 11:8,12 11:15 12:4 29:7 42:18 43:19 45:7,13 122:9 148:23 149:6,18 257:4				

assisting 187:2	asthma 48:17	Australia 388:3	295:15 296:2	295:19 305:10
assists 23:17	96:9 97:17	author 10:13	298:12,18	313:16 320:17
associate 7:14	100:23 102:12	224:9 225:8	306:22 310:11	320:22 325:11
94:5,12	103:3 104:17	253:6 290:14	367:13 385:17	338:17 351:22
associated 10:10	107:2,8,15	317:20 369:9	416:9	363:18 377:13
10:15 359:3	143:2 370:24	370:14 427:15	awareness 63:25	378:5 392:19
366:3 379:18	371:1 372:24	authored 290:18	231:23	396:18 400:4
380:22 389:4	372:25 373:12	authors 45:19	awful 70:7 237:5	400:19 426:20
428:6 462:18	373:15,20	240:13 245:15	343:10 462:5	435:25 441:10
association 11:8	374:8,18 375:1	247:12 272:9	awkward	441:14 442:14
127:10,19	375:19 376:7	290:6 365:3	116:23	446:17 447:14
148:17 271:20	Atkinson 397:23	370:12 413:7		463:5 464:16
273:15 278:3	attach 351:19	414:14 424:12	B	464:20,23
278:15 295:7	attached 6:9 7:2	425:20 430:16	B 1:15 2:1 6:2,8	465:22
295:18 302:12	8:2 9:2 10:2	448:6,25	7:1,9,14,20 8:1	background
305:20 322:17	11:2 12:2 26:1	451:22 452:17	9:1 10:1 11:1	90:18 100:15
352:25 361:23	42:5,14 43:7	453:3,16	12:1 13:22	175:14 255:10
362:3,4,7,22	298:16 308:23	454:19	66:4 470:20	284:9
362:23 384:7	439:25 442:14	available 49:4	474:11	backgrounds
394:1,23 402:7	472:10 474:8	49:15 212:18	baby 7:4 49:19	175:11 288:20
414:16 417:11	attaches 309:14	241:15 257:25	50:19 51:7,15	bad 277:6 414:5
422:23 423:8	attachment	258:2 271:21	52:9 53:4,13	450:15
445:22	18:12	271:23 272:10	53:13,25 54:1	baked 77:15
associations	attachments	277:18 278:5	54:12 56:16	146:15
236:19 368:1	18:15,21	278:17 279:24	58:18,23 74:15	balanced 217:4
assume 14:21	attack 107:9	293:13 322:13	87:17 381:19	237:4 238:4
21:13,18 70:23	attempting	383:22 384:4	385:12 413:9	343:7,14
71:4 76:1	274:2	456:12	back 14:9 16:22	Baltimore 2:5
78:16 79:16	attend 104:8,23	Avenue 3:21	19:14,16 27:19	10:17 13:9
80:8 132:25	105:1 232:12	5:11	39:8 44:19	Bank 3:22
135:21 147:4	232:15 261:5,8	average 47:14	50:19 52:22	Barnard 21:23
191:10 222:13	261:12,22	avoid 51:17	54:10,17 56:15	22:9
234:8 235:10	attention 14:19	54:19,20	57:4,13 58:3	base 302:11
242:2 246:4	45:13 83:9	award 92:3	70:8 77:24	356:20
288:2,18 295:5	100:6 121:3	aware 15:9	85:25 86:14,18	based 59:6
370:4 399:19	139:20 236:4	22:23 36:5	89:7 93:12	212:16 285:15
419:7 459:10	256:5 271:10	38:14 41:21	106:23 114:12	287:3 303:25
465:13	282:9 284:15	50:12,15 63:21	117:2,16 139:9	304:22 316:11
assuming 86:25	290:22 298:16	63:22 64:22	140:9,13	317:5 319:19
119:2 205:22	378:14 379:7	65:8 71:10,24	144:21 149:3	326:12 339:21
233:16 240:14	393:19 394:8	75:3,19 81:19	151:20 163:8	346:8 356:17
295:4 450:2	400:18 414:11	110:7 113:22	166:23 185:7	367:16,20
assumption 78:8	416:23	168:16 188:20	197:2 204:23	375:25 382:7
78:12 234:23	attorney 27:4,7	189:3 196:13	227:23 229:15	386:12 394:25
assurance 386:7	27:7 472:12	197:1,5 198:17	230:25 242:3	405:2 406:12
asterisk 332:20	attorneys 49:18	231:11,17	261:13 280:14	406:13 415:19
334:12 355:6	84:3	232:13 264:20	286:16 291:20	422:7 438:18

450:4	226:4,7 227:14	179:22,25	bits 287:1	147:5,14
bases 210:4	231:12 243:6	192:9,12,15	blackened 161:17	239:11,21,24
211:22,24	255:18 263:17	binder 164:25	180:3	268:11,15,23
238:11 242:25	306:18 318:9	164:25	blank 355:16	269:9,16
247:23 399:16	325:5 370:23	bio 151:10	blocks 285:17	270:14 271:1,4
basic 344:20	370:24 378:5	biologic 256:24	blog 312:14	362:22 419:8
388:24	428:13 432:22	272:25 273:4	blood 404:25	447:22
basically 105:4	442:2 453:13	433:20	405:25	brand 303:6
180:1 212:24	453:13	biological 384:6	Bloomberg	brands 381:25
352:18,22	belong 145:21	418:25 419:4	100:21 101:20	382:7,8 383:20
358:19 388:24	174:19	445:14 446:16	101:25	break 19:17
401:20 449:13	beneficial	446:19 447:17	blowing 44:7	62:9 77:11
basis 243:16	309:14	448:7 449:1	blue 389:19	88:22 133:6
253:16 288:4	Berge 237:25	biologically	board 94:16	151:10 158:7
345:20 381:3	238:2 454:24	89:22 384:6,20	bodies 209:2	164:2 178:15
392:7	best 37:13 38:5	385:22 414:15	239:7	181:23 204:10
Bates 8:17 9:21	50:17 104:3	415:22 416:6	body 11:9	204:10,12
Baylen 3:15	108:19 159:5	418:16 420:10	211:12,15	217:16 280:7
Beach 4:6	184:12 322:14	421:4 422:10	228:7,12 246:7	280:17 320:16
bear 65:25	333:15,16,18	424:13 425:22	412:18 417:17	320:17,25
122:8 181:25	444:13	432:10 450:7	434:12	377:4,5 426:10
bearing 123:16	better 93:15	450:20 451:23	boils 306:13	breathing 54:20
becoming	161:10 164:13	453:3,19 455:6	bold 174:18	breeze 44:7
454:16	180:11 353:16	biologist 253:20	book 290:17	Brief 251:24
Bedrooms 10:16	386:25 405:5	253:20,24	292:9	briefly 19:2
Beg 76:19	beyond 8:23	254:16,21	bottle 7:4 51:7	229:15
325:16 437:22	9:10 167:17,18	255:1,6,16	51:12 52:8,22	bring 16:24
beginning	296:25 308:18	454:19	52:25 53:3	27:23 34:7,9
177:17	309:3,22	biology 175:14	bottles 49:19	34:10
begun 102:20	bias 239:17,22	biomarker	50:1	bringing 100:6
behalf 3:3 4:16	biases 462:11	405:3	bottom 54:22	broad 48:15
5:15 55:17	BIDDLE 5:4	biostatistician	76:8 96:25	64:7 303:12,19
136:16 158:5	big 195:21	293:22,23	172:4 211:10	306:8 402:25
behavior 264:2	378:10 379:3	Biostatistics	256:7 284:16	407:1
264:3	bigger 306:12	314:12	284:17 344:25	broader 95:24
belief 59:1	bill 11:25 25:4,7	bit 24:24 27:4	350:15 393:20	broadest 415:2
395:20	25:10,13	59:21 73:12	396:4 444:17	broadly 147:11
believable	158:18,22,25	77:25 115:6	bought 54:5,5	broke 469:9
390:15	159:11,11,14	121:1 158:8	bounds 337:3	broken 332:23
believe 15:5	159:21 161:23	186:1 205:3	340:25	346:18 403:23
22:17 27:14	178:1,16,16,17	230:11 238:7	Bowman 311:7	bronchoscopy
31:17 43:14	178:22 179:4	241:23 245:12	313:13,14	123:12
56:3 82:7,16	438:9 439:2	314:18 341:13	Bowman's	brought 34:6
121:4,5 139:13	billed 40:3,6	352:24 360:19	296:4,6	169:25
177:16 209:23	159:22 160:1	370:24 376:21	Bradford 145:6	Brown 4:17 6:5
210:25 215:6	161:13	377:25 399:21	145:10,15,23	15:18 16:3,6
219:16 225:22	bills 25:2 158:10	407:16 468:12	146:2,11,18,20	18:4 19:7,15

Gregory B. Diette, M.D.

Page 480

19:16 20:22	103:18,21	167:4 168:19	232:7,17 233:1	314:10,25
21:17 22:7	104:2 105:10	169:4,7,13,20	233:4,12,15	315:5 318:13
23:19,22 24:10	106:6,22 107:4	170:15 171:16	234:2,17,22	319:19 321:10
24:14,17 26:9	107:16 108:8	172:11 173:18	235:5,7 236:25	321:21 322:9
27:11 28:21	108:23 109:4,9	174:6,10 175:5	244:2 245:25	322:21 323:21
29:1 31:6,22	109:18 110:1	175:12 176:2	246:10 247:24	324:22 325:2
32:8,13 33:6	110:12,15,24	176:15,22	248:7,17,23	326:3,6,10,17
33:14,23 35:7	111:5,11,19,23	177:9 178:12	249:6,11,17,24	326:23,25
35:17,25 36:24	112:5,13,24	178:24 179:8	250:6,21 251:5	329:12,17,20
37:14,17,20	113:2,9,12,14	179:17 180:5	254:17 255:2	329:25 330:4
38:1,8,11,14	113:18,22	180:25 181:9	255:15,22	330:22 331:4
38:18,21,23	114:1,13,16,20	182:18 183:1,7	256:1,17 258:4	331:18,22
39:1,6,11,19	115:1,4,13,25	184:4,18	258:14,25	332:1,4,7
40:16 41:15	117:11,20	186:10 187:10	259:8,10 260:5	333:19 334:10
42:8,19,25	118:1,25 119:9	187:20 188:5	260:10,25	334:20 335:5,9
43:12,20 44:13	120:17 123:25	188:11,23	261:2,16,24	335:12,16
45:5 47:6,22	124:23 125:8	189:2,21 190:8	262:19,24	336:2,21
48:11 49:5,21	125:14 126:21	190:22 191:21	263:20,24	337:11,15,19
50:4,21,24	127:13,21	192:4,10,12,17	264:4 265:2,20	337:22 338:2,5
51:9,19 52:23	128:21 129:9	192:20 193:1,5	266:1 267:18	338:8 339:4,17
54:2,14,25	129:15,18	193:20 194:1	268:2,12,18	339:25 340:6
55:8,16 56:2,8	130:2,11,15	194:11 195:5	270:2,5 271:7	340:11 342:18
56:19 57:14,23	131:5,11,17	195:14,18	272:2,16	343:18 345:7
58:14 59:5,12	132:12 133:10	196:2,7,10	273:23 274:1	345:11,22
60:4,17 61:4	134:21 135:3	197:13,17	274:17 275:4	346:8,13,17,20
61:13,18 62:4	135:16 136:10	198:7,21 199:3	275:13,15	346:25 347:12
62:10,21 63:24	137:9,22 139:5	199:16,18	276:3,13,16	348:5 349:11
64:6,9,14 65:1	140:5,11,23	201:12,15	277:20 278:7	350:14,19,21
65:12,19 66:18	141:13,18	202:5,9 203:3	278:11 279:8	351:3 352:3,10
67:15 68:11	143:3,6,20	203:7 204:9	279:13 280:3,6	353:11 354:4
69:14,20 70:22	144:1,4,20	205:10,17	281:8,15	354:16 356:3
72:8,19 73:7	145:7,16	206:10,19	282:21,24	356:25 357:13
73:15,18 74:13	146:13,24	207:18 208:20	283:4 286:10	358:8 360:13
74:17,24 75:8	147:8,18,23	209:3,9,20	287:6,25 288:3	361:24 362:10
75:10,17 76:18	148:18,25	210:11,17	288:9 289:2,4	362:25 363:13
76:20 78:20	149:15,23	215:16 216:10	289:8,13	367:8 368:19
79:2,21 80:16	150:15,21	217:21,25	290:23 291:13	371:19 372:1,4
80:24 82:1,11	151:6 152:11	218:6,12,15,19	292:1,4 295:23	372:14 373:3
82:17,22 83:2	153:17 154:10	218:23 219:11	298:20,24	373:17,22
83:13,21 85:3	155:1 156:6,16	220:17 221:19	299:2,12,21	374:9 375:8,10
85:9,14,20	156:19,24	222:8,25 223:7	300:1,6,12,15	375:14,20
86:2,11,24	157:10 158:11	223:24 224:1	301:18 303:1	376:16 378:18
87:1,8 88:5,7	158:14 159:3	225:2,17 226:2	304:3,8,12,17	380:4,11,24
90:1,15 95:11	159:13,23	227:12 228:8	304:25 306:6	381:3,20 382:2
96:17 97:22	160:7,9,16,19	228:13,21	307:1,7 308:3	382:16 383:6
98:7,11,13,15	160:23 161:21	229:22 230:19	310:5,8,18	384:9,22,25
99:6,10,15	166:1,4,9,11	231:3,19 232:3	312:14,18	385:5,8,15

389:9 390:1,20	453:22 455:7	162:14,15	41:14,21 45:8	220:13 221:7
391:4,19,24	455:16,23	188:11 218:15	45:9,20 46:1	225:5,13
394:12 396:8	456:18 457:1,7	218:17,20	46:23 51:18	226:12 228:17
396:15 397:8	457:23 458:21	314:19 337:16	55:7,15 59:10	233:23 234:15
399:4,23	459:4 460:19	337:23 338:9	59:18 60:3,15	234:21 236:17
400:14 401:10	460:22 461:10	338:11,12	61:3 62:3 63:8	237:19 240:16
401:13,16	463:20 464:5,7	349:5 353:3,4	63:12,18 75:6	240:24,25
402:10,18	464:9 466:4,11	443:9	76:3,14 79:11	241:5,9 248:5
403:8 405:8,12	466:25 467:12	call-in 97:3	79:15 89:24	250:4 253:20
406:19,21	467:14,17,20	called 31:17	90:14,20	253:23 254:14
407:10 408:4	470:4,10	55:2 93:22	104:24 109:22	254:16,21,25
408:23 409:13	Brown's 18:8	95:7 118:20	111:3,10	255:6 263:16
410:5,8,19	55:20	146:20 152:22	115:24 116:7	271:20 272:15
411:1,13,18	Bruce 7:13 16:8	186:2 244:14	117:1,4,19	273:22 274:15
412:1,19	built 323:15	290:18 296:25	118:10,21	275:2 276:2
413:14,25	bulk 240:20	361:3,5 460:2	119:3,7 122:7	278:4,23 279:3
414:4 416:13	bullet 303:23	calling 306:16	122:8,19,21,24	285:18,21
417:25 418:19	bulleted 181:21	calls 60:18 75:10	123:6,8,13,14	359:4 364:1,11
419:6,15	bullets 469:9	110:15 158:14	123:18,19,23	365:5,16 368:3
420:13,18	bunch 70:13	178:12,24	124:18,22	368:18 372:4
421:6,14	91:25 253:2	186:10 188:6	125:3,7,13	376:15 378:1
422:14,25	369:5 376:9	191:6 229:23	126:5,10,15	379:11,17
423:4,11	435:25 460:13	230:20 231:4	127:12,20	380:3,21 384:8
424:15,21	bundle 86:16	235:8 261:2	129:7,13 130:1	384:21 385:24
425:23 426:2	Burden 8:17	309:4 430:8	131:1,14 132:8	386:11,19
427:25 428:3	281:25	435:5	134:10,16,19	387:6 388:7,25
428:18,25	Burge 454:24	camera 19:19	135:6,15 136:8	389:5,8,19
429:14,21	business 24:21	113:16 378:17	136:17,20,21	391:3,11,17,23
430:1,7,12,20	178:19 191:11	cameras 19:17	137:21 138:8	392:8 394:2,24
431:10,13	193:11 266:14	Canada 8:14,14	140:22 142:12	395:13,23
432:5,14	buy 50:9	264:22 265:17	147:22 148:17	397:17,18
433:13 434:3		266:5,11,18	149:22 150:13	398:1,1,2,2,10
434:21 435:5	C	267:6,15	150:20 151:4	398:11,14,15
435:19 436:15	C 3:1 6:1 7:8	268:10 272:13	163:3,7,14,19	398:23,24
436:17 437:3	10:25 13:1	273:20 274:12	164:12 165:25	399:11,11,15
438:11,16	121:4	275:25 278:10	167:3,12	399:18 400:20
439:18 440:3	C-reactive	279:1 409:3,10	172:24 187:7	401:9 402:8
440:12,15,19	423:13	409:18,20,23	199:12 200:1,4	404:4 406:13
441:18 442:1	cake 341:10	432:2,9	200:6 201:5,10	407:8 410:18
443:18,22	CALCAGNIE	cancer 6:24 7:23	201:24 202:22	411:4 413:12
444:7,9,12	4:4	9:16,20 10:5	202:23 203:2	415:9,24
445:4,17 446:5	California 4:6	11:5,6,9,10,13	209:19 210:23	417:12,15,20
446:22 447:18	call 39:10 74:8	12:6 28:14,19	211:20 212:22	420:5 421:8,8
448:11 449:5,7	81:23 106:3,4	34:24 35:5	214:4,11,12,25	421:10 422:24
450:9,16,22	113:24 114:2	36:6,7,9,14,15	215:9,15	423:10,15,18
451:10 452:1	136:19 152:7	36:20,23 39:16	216:22 217:11	423:20 439:13
452:20 453:7	157:6,24	40:13,21 41:11	218:4 219:9	443:12 444:23

451:25 453:5	118:9,9,14	142:9 144:14	279:25 361:23	391:23 392:8
454:18 456:25	119:2 123:17	245:11 246:15	362:4 379:10	399:17
457:6 460:12	career 288:11	247:4,16 251:4	394:23 402:7	causing 76:3
462:19 464:4	careful 224:4,21	267:25 268:7	445:22	376:6
466:23 467:5	247:13 372:16	270:9 286:20	causality 60:2	cavity 433:8
cancer/ 198:25	410:19	288:11 325:6	265:19 275:25	435:2
cancers 61:2,6	carefully 194:13	325:12 343:6	362:24 363:12	cease 295:20
358:4	395:10 472:2	345:23,25	419:1 446:2	cell 358:4
candid 332:12	carrier 141:22	355:22 356:14	451:9	444:18
capacity 411:12	carries 94:11	360:5,21	causation 6:20	cell-based 252:8
capture 205:20	244:10	368:21 428:7	7:17 133:25	cells 422:1,1
250:1 447:22	case 37:10 38:2	455:14 460:3	148:22 149:4	cements 284:12
carbon 412:9	38:19 42:7,16	461:5 462:5	206:15,25,25	center 7:23 15:6
carcinogen	42:17,17 55:9	463:15	207:1,11,14	63:7 95:22
77:22 215:8	65:14 70:17	cases 1:11 36:20	239:10 277:10	96:4 100:8
225:24 226:9	78:3 80:2	39:16 40:13	362:8 446:14	104:23 214:4
382:25 384:5	81:17,18	55:7,15,15	463:13	215:15 224:25
384:15 399:22	110:23 111:1,2	135:15 136:7	causative 126:9	225:6,13
400:13 458:20	111:10 112:2,8	136:17 137:2,6	439:13	228:17
466:1,19,24	112:11,18	137:17,18	cause 34:24	certain 16:24
carcinogenesis	132:11 136:20	139:12,16,22	54:20 59:18	28:8 126:3
418:11 421:5	136:21 138:1,4	140:20,20	89:24 90:7,13	244:25 268:23
433:6 439:11	138:6,7,9	157:17 163:14	102:12 107:14	316:12 358:3
carcinogenic	146:7 162:12	167:3,8,20,24	126:5 240:18	449:23 467:4
215:6 225:23	163:3,9 167:10	181:4,6 185:23	278:16 279:2	certainly 16:20
401:2 402:1	181:6 194:22	186:16,17,19	370:22 376:14	21:19 48:21
carcinogenicity	197:1 199:11	186:21,24	383:11,15	56:10 90:24
420:11 422:11	199:19,24,25	187:14,15	384:20 385:23	100:2 104:17
carcinogens 8:9	206:1,25	199:1 200:7,18	386:9,11,18	108:1 129:21
10:25 120:12	207:10,14	200:21 201:4	387:11 388:12	143:7 149:5
231:15 235:25	209:12 219:5	203:5,18 207:3	391:3,11 401:9	164:18 166:10
260:22 465:5	232:14 240:10	239:14 244:6,7	407:8 415:8,24	201:18 222:17
467:8	243:25 244:6	244:8 247:23	432:11 450:21	226:3 260:1
carcinoma	245:13 247:13	248:2,6,10	451:24 453:5	261:4 294:18
428:7	251:15,16	251:3,11	456:25 457:6	352:8 363:6
Cardiology 10:8	255:20 267:16	268:25 331:11	457:14,22	367:21 388:5
cardiovascular	286:18,23	341:17 395:11	467:5	413:21 433:17
10:10 367:4	334:25 336:8	395:23 408:14	caused 313:15	451:16 453:2
care 34:19,22	336:11 345:5,5	categorically	359:3	463:4
62:1,1,2 63:6,9	345:17,17,21	255:5	causes 35:2,6	certainty 452:24
63:15 93:21,23	358:14 399:22	category 100:14	41:20 76:14	certificate 471:1
94:17 96:11	401:8 459:24	162:10 292:8	109:21 125:7	471:13,19
104:10 105:8	461:18 468:6	causal 211:16	125:21 148:23	certification
105:12,13	469:15	212:20 271:22	206:8 219:23	94:16 471:20
110:11 115:23	case- 131:21	272:11,14	220:2 278:19	certified 119:25
116:6,10,17,25	142:5	273:21 274:13	278:22 279:17	471:1,2
117:18,24,25	case-control	275:1 278:6	373:12 374:18	certify 471:3

474:3 certifying 471:24 cetera 430:17 chance 17:2 20:17 71:12 99:8 193:9 299:10 305:12 Chang 351:11 change 8:14 77:17 93:8 206:8 257:16 280:9 313:19 317:4 320:6 340:24 344:1 344:20 383:21 384:2 473:4 changed 93:24 174:15 257:12 changes 79:6 472:8 474:6 chaos 315:17 Chapter 290:1 292:9 characterizati... 271:24 273:13 characterize 260:12 369:25 370:4 382:5 characterized 370:1 charge 24:19 25:17 177:17 177:22 178:7 197:11 198:5 213:19 charged 23:14 23:16 37:25 40:9 charges 178:10 197:21 chart 9:19 247:16 251:4 324:2,16 328:17 329:11 333:2 334:7,8 336:19,23	339:15 341:22 344:22 346:3 347:1,4 355:20 443:9 check 376:23 checks 196:1,9 196:12,19 chemical 8:12 285:23 286:8 chemical-relat... 187:15 chemically 286:12 chemicals 203:17 chemotherapy 63:5 Chen 351:10 cherry- 304:17 chief 81:12 child 58:11 404:11 child's 54:19 childhood 389:4 389:20 Children 10:18 chorus 446:8 chose 97:25 98:4 170:14 246:25 339:21 341:25 CHRISTOPH... 3:12 chronic 96:9 97:16 101:10 103:5 126:3 413:8 417:19 418:6 419:25 419:25 420:2,9 421:3 422:5,11 423:17,19 425:21 chrysotile 458:9 458:17 chunks 181:23 378:10 cigarette 404:21 456:24,24	cigarettes 404:12,17 circle 140:19 292:10 346:6 347:7,21,22 348:13 353:9 353:14 354:6,9 365:18 circling 348:9,9 348:17 351:16 351:24 circumstance 303:21 circumstances 319:11 359:5 387:7 394:18 citation 418:4 433:14,22 434:7 citations 468:22 cite 241:14 273:2 390:5,13 418:8 cited 222:12 252:18 253:3,3 337:5 364:15 364:22 390:10 390:10,11,11 390:12,12 412:3 448:15 cites 43:15 237:24,25 285:8,9 395:6 citing 222:15 237:8 285:21 361:5 city 48:18 102:17 374:21 claim 291:4 claimed 292:13 293:5 clarification 25:1 27:3 40:11 130:10 179:5 clarified 167:8 clarify 20:12	23:12 40:2 55:11 99:2,5 99:12 103:22 104:5 122:2 130:14,16 clarity 58:10 184:7 classification 260:22 classifying 439:12 clean 254:20 clear 26:10 32:16 38:9 105:12 106:25 114:13 132:2,3 161:22 163:6 168:8 184:23 195:20 209:16 245:16 252:12 271:22 305:18 310:4 358:12 433:19 455:25 468:4 clearly 394:24 clicked 311:5 client 155:7 157:3,6 190:14 191:15 192:2 193:10,16 194:6 196:5 clients 155:12 155:18 156:5 189:15 Climate 8:14 clinic 63:10 104:16 105:8 105:12,12 clinical 9:8 100:23 128:4 128:10 246:21 294:7,14 308:16 309:20 310:12 317:8 428:9 clinician 59:1 103:14	close 102:15,16 352:17 CMO 38:2,15 113:7,23 114:3 coach 78:25 83:20 304:6 coaching 156:12 332:3 coeditors 309:8 coffee 88:20 cognizant 252:13 COHEN 3:20 cohort 141:12 141:14,23 142:1,11,15,19 144:16 146:7 233:8,11 238:3 245:6 246:6,15 267:16,24 268:7 286:19 325:6 358:19 360:4 394:25 459:23,25 460:10 461:6 461:18,23 462:4 cohorts 233:3 238:8 247:5 286:22 coinvestigators 232:25 cold 44:7 collating 468:19 colleague 82:23 153:1,8 colleagues 303:7 352:14 361:1 463:17 collect 157:21 404:23 collected 404:24 collecting 157:18 collection 242:24 collects 159:8
---	--	---	--	--

College 94:21 239:4	317:8 337:1 342:11,11	208:4	392:7 396:10 396:13 413:18	239:17,22 462:12
column 45:18 394:8 414:20 444:16	343:12	completely 47:9 291:8 292:19 336:21 363:3	413:21	confuse 168:6 confused 24:8 308:21
com- 112:22	communicating 223:21	completing 470:18	conclusions 278:9 302:11 303:11 379:7 401:1	confusing 333:23 334:1
Combine 439:8	community 120:10 188:22	complicated 62:16 405:13	conclusive 273:8	confusion 24:6 245:13
combining 425:5	208:15 209:1 209:17 229:21 295:20 407:25 408:12	complying 114:1	condescending 113:17	Congress 235:4
come 21:2 77:24 104:1 106:13 108:12 152:21 164:25 170:18 177:23 203:20 227:22 278:19 286:16 288:19 325:22 363:17 430:19 431:5	companies 441:21	comprehensive 7:23 214:4 215:15 224:25 225:13 228:17 238:25 264:24	conditions 106:21	conjunction 44:2 179:6
comers 105:3 365:24 381:25	company 81:24 84:15 88:12 109:16 110:7 152:8 185:18 190:15 441:23	concentration 386:15 459:16	condoms 359:7	connection 211:16 361:23 469:15
comes 80:2 90:8 96:20 172:1 191:14 196:14 205:22	company's 441:14	concentrations 10:16 371:15	conduct 319:15	connotation 71:22
comm- 229:21	compared 236:17 365:14 366:23	concept 306:24 383:8,9,23 447:3	conducted 147:21 151:3 168:3 231:14 409:11	consequences 10:19 40:25 63:11 378:6
comment 179:22 216:15 267:2 356:9 358:25 409:4	comparison 11:6 397:18	concern 298:13 310:16 409:10	conducting 318:15	Consequently 271:24
commentary 306:17 317:23	compatible 235:13 237:2	concerned 80:3 184:1,2 362:16	conferring 58:8 138:19 211:3 213:5 267:10 282:1 296:20 376:19 412:12 426:8 437:14 443:4 447:7 459:21	consider 22:9 29:17 122:6 229:16,19 231:1 252:2,16 267:23 318:15 322:5 419:3 442:8 445:8
comments 14:5 14:11	compelling 439:7 441:16 441:24 442:9	concerns 428:14	confidence 305:22 317:2 327:18 328:19 329:7 330:11 337:3 340:25 341:1 353:8,9 354:2,10,11 355:3 357:9	considerations 146:19 239:11 363:2
commercial 73:22	compete 320:4	conclude 212:20 303:24 304:21 305:2,19,24 322:17 323:18	confidentiality 156:8,17 187:11	considered 6:22 19:6 20:5,7 22:4,12,14 66:3,8 245:20 249:23 253:12 392:12,14 395:10 396:2 435:12
commission 164:19 240:7 474:17	competent 132:25	concluded 274:13,25 379:24 391:22 425:21 449:3 470:21	confirm 197:9 422:4	consistency 270:23 292:8 292:11 321:6 322:4 357:22 359:9
commissioned 266:24	competition 456:7	concluding 272:22	conflict 196:6,15 196:19,23 305:24 323:18	consistent 32:2 271:17 272:3
Committee 231:13,13	complaint 110:23 111:6,9 111:25 112:16 196:16,17	conclusion 212:10,11 277:3 278:12 279:22 283:24 285:14 323:13 379:12 380:19 381:2 382:14	conflicts 196:1,9 196:12	
common 10:14 49:13 292:12 369:3,7,7 443:11	complete 21:8 86:24 99:23 191:18 206:5 244:20 310:18		confounding	
communicate	completed 131:19 135:9,9			

278:1,2 357:21 359:2 consistently 172:9,23 236:13 237:14 271:19 272:3 consists 77:13 constituents 211:18 consult 106:4 225:13 233:9 consultant 188:2 consulted 105:25 consulting 117:25 135:18 136:11 152:8 consumer 8:7,9 231:14,16 232:11 235:24 235:25 consumers 78:18 80:14 84:22 87:20 223:14 contact 54:20 174:20 184:15 284:6 contacted 185:13 contain 75:5 78:4,11,17 84:6,17 211:19 contained 6:15 17:15 54:23 57:4 70:19,20 71:7,19 87:24 92:14 127:9 162:21 170:4 208:8 248:21 249:3 285:24 336:1 382:12 382:13 436:11 containing 401:4,8,24,25 contains 51:16	210:4 215:7 225:23 contaminated 383:2 contamination 283:11 content 176:14 177:8 191:9 309:9 context 46:10,12 83:16 111:3,4 134:20,25 156:24 170:20 180:20 193:19 193:22,22 200:3 263:5,7 321:22 378:20 419:8 continue 150:9 337:15 430:23 Continued 4:1 5:1 7:1 8:1 9:1 10:1 11:1 12:1 continues 50:13 453:7 continuing 292:1 contract 154:17 155:5 contracted 154:23 159:20 159:25 contractor 153:21 154:8 155:16 176:21 contracts 33:1 33:19 contrary 215:13 contributed 20:8,11 395:13 contributions 468:9 contributor 444:22 control 9:17 142:6 146:8 267:16 286:23	471:23 controls 224:8 245:13 248:12 251:15,16 331:11 336:9 341:18 345:5,6 345:17,17 356:16,17 358:15 461:18 conversation 173:22 174:2 176:6 266:12 342:22 conversations 175:22 176:18 176:24 conveying 33:2 Cook 351:11 cooking 374:24 Cooper 185:11 185:13,18 186:8,18,22 194:22 195:3,4 195:12 cooperation 26:16 COPD 96:10 103:3,4 104:17 143:1 copies 31:3 165:2 378:3,19 427:2 437:17 copy 17:13,23 32:5 82:14,21 85:21 86:12 88:17 91:3,3 112:16 134:8 139:3 140:11 154:4 312:12 325:15,17 348:18 393:5 397:7 426:24 430:11,14 431:19 471:11 corner 285:1 419:13 cornstarch	334:18 335:1 337:7,13,14,18 corporate 4:5 192:2 194:5 Corporation 110:11 correct 15:3,7 15:17 18:3 20:21 21:16 25:5,6,8,9,11 25:14,19,20,22 27:20 28:25 30:23 31:13,14 31:19 33:22,22 33:23 34:19 40:7 43:16,17 48:20 49:4 52:16 57:22 58:13 61:3,8 67:2 79:13 84:13,18,19,19 84:24 88:4 90:25 92:7 93:20 94:21 95:2,21 96:13 96:14 98:18,19 100:15 101:2 108:6,22,24 120:18,25 121:12,23 124:19 126:11 126:16 127:7 127:15 128:5 131:2,3,6 134:4,11,16,17 135:11 136:2,8 140:17 142:13 142:17,21 144:19 145:4 150:4,7,10,13 150:14 151:5 154:24 159:9 159:10,22 163:5 174:5 177:18 178:7,8 178:11 179:7 179:15 181:7	181:10 183:8 193:14,15 201:11 203:12 205:11 206:9 207:2,4 208:5 209:7,21 211:22 213:1 214:4 222:16 222:17,24 229:14,17 232:1,2,6,8,22 242:4,5 247:6 248:4,16 249:4 254:22,23 255:14,21 257:23 258:23 260:19 264:12 268:8 290:11 290:13 293:20 294:15 305:10 305:13 306:21 308:1 324:13 325:7,14 329:11 339:3 339:11,12,15 340:2 342:17 345:6,18,19,21 346:1,16 349:12 351:9 352:9 354:13 356:24 357:11 360:9,12,22,23 362:5,24 363:20 364:23 364:24 367:2,7 368:18,25 369:1 370:6 373:1 378:25 380:22 381:21 382:1 384:15 384:16 391:17 392:15 393:18 393:23 394:3 396:13 398:12 399:24 402:15 403:15 407:13 409:6 413:5
--	--	--	--	--

417:7 418:13	37:19,21 38:17	350:14 376:19	205:8 246:9	93:21 94:17
419:10 423:23	38:22 42:8,8	377:22 390:1	247:2 259:3	96:11 264:22
425:15,17	42:12,25 47:13	397:6 408:5	330:16 339:18	319:25
428:19 432:3	52:23 53:2	412:12 419:16	397:9 430:1	critically 105:14
434:13 437:24	57:23 58:8	420:13 424:15	court 1:1 2:17	criticisms
440:8 444:6	61:13 62:21,24	426:8 437:14	13:14,19 71:17	460:23
446:2 452:8	65:21 66:18	438:4 439:16	112:18 134:9	criticize 118:14
455:22 456:17	68:13 70:23	443:4 447:7	146:1 156:10	460:1 462:9
459:24 465:2	78:20 80:17,21	459:21	161:2,3 205:15	critique 256:24
467:10 471:11	80:21 82:11,19	counsel's 77:4	341:25 407:22	crocidolite
474:4	82:20 83:13,19	count 60:21	472:15	388:4 391:10
correcting	85:3 86:2	137:13 299:6	courtesy 39:4	457:13 458:11
101:18	88:16 89:10	404:17 454:19	114:10	CROSS-EXA...
correction 77:4	98:10 99:8,10	456:15	cover 206:22	464:24 467:19
272:7 330:19	100:9 103:22	counter 237:22	441:2	crossroads
400:11	109:10 112:13	counting 455:15	coworkers	113:5
corrections	113:9,11	455:25 456:7	404:6	crummy 343:3,4
472:3,5 474:6	114:14,18,20	countries	Cramer 222:14	CSR 471:18
correctly 45:22	114:25 115:1,3	367:14 374:25	286:1 351:10	cubed 376:1
77:3 88:1	126:21 130:17	country 249:9	351:10,11,12	404:21
97:18 100:25	132:16,25	couple 20:15	351:14 427:16	cumulatively
101:12 102:24	133:10 135:21	27:5 97:25	462:22	391:9
103:9 236:21	136:10 138:19	100:3 108:17	crazy 269:20,23	cure 39:18 40:15
272:1,6 282:17	139:4 140:6	116:8 130:7	269:24,25	curious 257:8
286:6 292:17	154:3,12 159:3	137:14 143:22	270:7,15 271:2	316:22 323:11
292:22 301:14	160:12,22	164:17 175:1	create 168:23	current 91:19
302:8,15 306:3	161:2,21 166:1	201:23 230:2	198:13,13	93:18 97:21
370:9 379:20	166:16 169:4,6	230:23 231:1	224:11 250:10	257:22 319:14
395:17 417:21	193:6 204:10	247:11 250:13	250:14 266:3	currently 128:3
420:6 428:11	211:3 213:5,6	253:13 259:3	created 170:20	128:9,19,24
439:14 468:22	217:22 218:10	264:21 269:12	267:1 287:14	129:2,5 136:6
Correlative	218:12 227:12	272:24 291:16	346:9	137:5 187:3,4
11:16 427:10	227:24 228:4	293:3 300:4,9	creating 468:22	203:2
correspondence	234:3 255:23	300:22 308:13	credentials	curriculum 7:9
166:14	267:10 273:25	314:1 332:18	188:16 288:21	91:3,10,24
cosmetic 75:25	275:15 277:20	386:5 392:18	credible 224:12	92:9 127:10,18
76:13 285:24	280:3 282:1	456:21 458:17	255:7 260:15	142:24 146:9
286:9	287:7 290:23	462:20 463:23	260:17 315:13	364:21 390:9
cotinine 404:23	292:3 296:20	464:10 467:23	316:13	curve 458:19
406:8	299:21 304:6	couple-year	criteria 93:23	459:3 465:5,14
counsel 7:5	312:11 324:22	408:1	239:9 245:24	465:16 466:2
13:18 17:8	326:5,15,21	coupled 452:24	246:18 271:18	466:20 467:8
19:7 24:11	329:14,16,17	course 19:19	278:2 307:23	customers 79:20
26:9 27:11	329:19,22	42:2 62:24	358:24	cut 61:19 275:16
31:3,23 33:6	330:2,6,25	106:12 155:14	criterion 269:9	336:3 337:15
33:11,20,23	335:12,13	160:24 166:16	292:11 419:2	cutting 337:11
35:17 37:15,17	336:3 338:4	167:5 189:17	critical 34:19,22	CV 88:17 92:6

92:21,23 93:4 108:13,15 121:4,9,9 126:22 127:4 128:2 142:24 143:9 CYNTHIA 4:3 cytokines 444:19	21:20 22:11 23:1 68:9 121:9 235:25 308:19 328:6 369:14 438:25 Daubert 6:20 7:17 70:24 71:13 133:25 206:15 207:16 207:17 day 21:21 39:5 158:2 195:9 264:18,19 275:16 313:19 327:6 404:12 404:16 407:18 427:2 431:11 437:16 474:16 days 158:3 472:12 deal 106:13 123:22 128:13 128:16 142:25 143:24 dealing 106:15 106:16 132:6 134:9 deals 48:22 106:19 dean 294:7 death 34:25 35:2 35:6 deaths 36:6,14 debate 78:13,15 303:5 decades 230:2 230:23 231:1 302:7,25 303:8 303:8 December 8:15 decide 27:9 161:3,3 332:17 339:13 decided 316:14 319:1 352:15 decision 333:11 399:16	decisions 301:7 303:14 306:2 368:5 declare 316:12 decrements 371:15 deemed 472:15 defend 184:17 184:21 DEFENDANTS 4:16 Defendants' 6:14 17:14 defending 132:25 defense 60:22 defer 254:15,24 deferring 255:4 255:19 256:14 define 73:5 definitely 22:10 283:10 378:9 definition 262:21 361:6 447:16 definitive 221:14 degree 94:23 95:6 degrees 175:15 deletions 91:23 deliberately 247:8 deliberating 261:14 deliver 164:21 demonstrate 352:2 demonstrated 412:24 422:11 425:11 463:24 464:3 demonstrates 282:12 283:8 demonstrating 270:20 demonstrative	324:16 325:25 denigrate 461:20 DENNIS 3:19 dep 172:7 department 11:21 15:9 34:18,20 47:21 56:13,14,14 93:4 94:3 100:20 118:23 118:23,24 119:1 314:12 Departmental 7:15 departure 271:23 depended 402:8 depending 403:19 404:25 depends 164:24 191:10 196:18 197:18 263:5 318:21,22 321:14 402:23 402:24 depo 172:8 deponent 13:16 474:1 depose 114:25 deposed 81:17 deposing 472:12 deposited 449:15 deposition 1:14 2:1 6:10,12,16 7:3,6 8:3 9:3 10:3 11:3 12:3 13:8 14:5,11 14:13 15:11 16:13,18,23,25 17:16 18:3 22:12 26:12,13 27:20 29:1,14 31:16 34:6,11 38:18 45:3 60:7 66:19	81:21,22 82:13 82:14 83:15,17 83:23 84:4 85:2 86:10 88:17 111:16 114:7,9,19,21 133:1,2 137:19 138:8 154:12 156:11 157:25 160:23 165:9 167:24 177:17 231:21 257:20 258:22 296:4,7 296:13 311:8 313:13,15 341:6 439:9 470:18,19 472:2,10,13,14 depositions 15:16,21 21:5 38:3 65:11,17 67:20 132:15 133:4 137:16 139:23 165:6 165:12,15 256:11 derivative 198:11 derived 271:23 dermal 266:20 describe 24:3 119:23 244:11 described 182:24 200:16 209:14 355:21 360:20 456:10 describing 196:21 388:23 description 74:7 189:24 244:16 deselect 244:25 251:22 deserves 292:12 design 288:12 343:10 358:21 447:3 461:25 designs 144:19
--	--	--	--	--

267:15 461:20	62:3 63:17	133:20,23,24	470:13,20	difficulty 319:17
desist 295:21	115:24 116:7	135:16 138:15	474:11	digest 300:23
destroy 112:9	117:1 118:10	138:23 139:11	Diette's 32:2,6	digit 458:16
285:10	118:21	151:22 156:9	difference 35:4	direct 13:25
detailed 256:9	diagnosis	159:7 160:6,10	207:7 252:9,14	45:12 65:25
271:16 277:25	124:21 423:15	160:15 161:7	305:20 322:18	83:9 85:5
details 69:16	dial 106:23	161:17 169:10	420:21 429:25	121:3 236:4
detect 46:22	diaphragm	170:13 172:17	430:5	268:17 271:9
detectable	339:10	180:11 182:23	different 28:2	271:10 282:8
283:19	diaphragms	184:3 189:8	51:11 59:16	284:15 290:21
detected 39:17	339:10 359:7	192:25 193:8	60:1 65:13	338:1 378:14
40:14	dictate 173:4,10	193:18 204:25	73:2 90:6	393:19 400:18
detectible 284:7	173:13 363:12	205:2 206:13	91:17 93:15	414:10 416:23
detection 47:2	363:14	206:15 208:2	94:11 104:8	433:5 471:23
286:2	die 36:22 41:4,9	213:9 215:12	118:24 119:1	directed 444:23
determination	diet 102:21,22	219:5,14	121:24 124:1	directing 394:7
396:3	108:4	220:10 231:11	143:8,9,16	direction 50:23
determinations	dietary 102:20	235:18 264:9	148:1 168:13	directly 158:20
339:2	108:3	267:8 273:19	170:20 174:12	158:25 195:4
determine	Diette 1:15 2:1	280:16 281:19	176:22 178:16	284:4 406:11
191:16 402:17	6:2,10,12,17	286:17 289:22	200:25 203:19	449:15
405:10 450:20	6:19 7:3,10,13	290:1 297:14	205:22 213:20	disagree 45:24
determined	7:14,16,21 8:3	297:18 304:16	217:18 219:25	88:3,9 216:14
365:3 389:3	9:3,15 10:3	308:7 310:11	220:2 222:23	217:7,8,15
398:21,22	11:3 12:3	312:9 320:24	224:15 241:6	219:21 223:4,6
402:6 453:17	13:17,22 14:2	324:17,18	250:16 253:3	223:9,10
determining	14:10 16:6,9	325:4 326:1,20	258:9 263:2	233:25 273:19
251:3	16:12,14,17	326:23,24,25	266:19 282:5	274:11 275:24
develop 46:21	17:19,22,24	327:1,3,10,24	291:24 320:1	276:19,19
48:6	18:22,24 19:19	330:7,10	323:25 335:2	380:18 420:20
developed 48:23	20:3 27:12,18	332:10 338:20	336:8 339:9	432:2,12
375:1	34:13,23 37:8	355:20 360:2	340:9 342:12	disagreeing
developing	39:14 42:14	366:11 369:3	342:21,21	392:1
46:25 233:22	44:20 45:1,2	369:16 377:16	349:15 354:21	disaster 171:1
234:14,20	45:16 46:20	377:19,24	357:21 382:6	discern 357:20
236:17 237:18	52:8,11 54:6	381:15 391:2	387:10 389:23	disclose 135:19
263:13 372:18	54:10 55:5	393:1 397:1,4	396:12,14,16	156:9 166:13
372:25 374:25	57:8 58:25	399:13 403:1,2	400:9 401:11	430:15
376:11	62:23 63:20	403:4,14	403:7,19	disclosed 135:19
development	66:9 67:20	410:17 411:8	404:18 412:6	135:22 136:4
46:13 417:20	75:3 82:9 83:8	413:23 416:19	412:10 423:14	137:10 156:10
420:4 444:22	87:5 89:9,14	422:8 426:23	433:2 436:20	203:8
develops 47:18	91:5 95:14	427:5,8 431:14	436:20 451:14	disclosing
devoted 298:16	98:18,24	437:19 438:24	453:9	187:12
diabetes 107:8	100:18 102:2	441:1 442:22	differently	disconnect 43:1
diagnosed 39:17	115:16 117:22	465:1,25	177:20 241:3	436:10
40:14 60:15	123:20 133:6	467:21 470:11	451:15	discuss 127:4

173:16 174:10	disparities	133:16 137:9	380:25 381:4	466:2
176:16 260:22	103:8	140:25 141:23	402:5 430:8	dose-response
298:10 309:12	disparity 286:22	146:25 159:3	434:4 438:10	358:1 458:19
309:25 432:9	dispense 14:4,10	166:12 177:2	438:24 440:5,7	459:3 461:3
discussed	displayed 87:7	187:10 190:10	441:23 442:3	462:18,21,25
157:17 176:25	disputable	213:12 229:8	documentable	463:1,2,10,19
260:24 338:22	433:21	237:10 256:4	282:16	464:3 465:5,14
453:3	dispute 415:7	268:19 270:5	documentation	465:16 466:2
discussing	429:6 434:2,5	274:8 275:6	31:24 33:8	466:20 467:8
141:11	454:1,2 467:7	282:24 304:4	documented	doses 459:15
discussion	disputing 381:2	304:11 305:7	273:2 336:25	dotted 349:18
314:17 338:15	381:6	308:10 319:22	342:2	350:9
377:15 416:23	disregard 287:2	326:13 328:2,4	documents 18:2	double 132:24
440:24 454:21	287:11,13,18	329:13,23	21:15 34:3	doubled 215:4
464:21 467:18	321:7	331:21 332:10	161:22 253:4	222:5 223:18
467:25	disrespectful	335:4,8 337:10	260:15,17	doubt 96:20
discussions	219:17	347:4,13	449:8 468:23	129:20 182:4
173:20	disseminating	351:16 378:24	doing 21:4 38:3	291:22 463:22
disease 9:16	309:21 434:25	381:6 399:12	38:12 40:3	dozens 423:14
10:10 41:4	dissemination	414:8 416:22	63:19 83:13	Dr 8:4 13:16
46:14 90:8	434:18	426:6,9 431:2	99:13 135:17	14:2,10 16:6
96:9,11 97:15	distinct 245:18	437:17 438:14	153:7 155:6	16:12,17 17:22
97:16,17	distinction	440:11 447:16	163:25 187:13	17:24 18:22
100:24 101:9	357:18	448:4 468:4	192:15 197:2	19:19 20:3
101:10,11	distorting	doctor's 27:13	275:15 316:6	27:12,18 32:2
103:5 104:18	362:16,18	346:11	320:8 321:1	32:6 34:13,23
104:22 106:20	distracted	document 1:10	326:22 327:3	37:8 39:14
107:9 122:11	394:10	6:15 7:8,11,19	342:14 350:2	42:14 45:1,7
143:1 148:24	distribute 49:20	7:22 8:4 9:15	352:13 376:22	45:16,18 46:20
263:14,23	distributed 50:2	16:18 17:14,25	386:25 403:2	52:8 54:6,10
372:2,13,16,18	310:13	18:5,13,19	405:22 408:2	55:5 57:8
372:20 376:11	District 1:1,2	19:4 20:4 32:1	425:4 428:24	58:25 62:23
383:11,15	13:14,15	32:14 36:10	451:11 472:6	63:20 67:4,14
388:13 450:6	diverge 73:12	37:3 213:14	dollars 408:2	67:20 69:10
450:21 451:8	diverse 236:19	224:2 225:3	Don't 302:1	70:18 71:7
467:5	divide 458:12	247:21 267:1	dose 80:2,4 90:9	75:3 81:7,16
diseases 61:2	division 34:21	274:2 275:5	125:23 126:6	81:22 82:12
101:4 103:3,25	93:20 310:12	276:4,22 277:5	386:7,8,9,10	83:8,15 84:4
104:20 121:22	divorcing 80:17	282:25 290:24	386:11,15	87:5,16 88:4
122:6,10	doc 61:20 63:7	297:6 300:7	391:2 392:9,20	89:9,14 98:18
123:23 142:3	doc- 216:1	304:12 306:24	402:2,8,17,19	100:18 102:2
143:5 150:2,7	doctor 26:19	308:12 311:19	403:4,6,8,17	115:16 117:22
367:4 387:12	35:21 39:6	312:13 326:7	404:1,1 405:2	123:20 133:6
388:6 415:16	42:6,21 83:2	330:17 332:8	405:17 406:18	133:23 135:16
dish 252:8	83:15 85:16	341:21 346:9	421:20,21	139:11 151:22
dismantling	87:12 97:4	346:11 347:8	457:18 458:11	156:9 159:7
471:12	99:18 130:14	378:21 379:4	465:9,15,15,17	160:6,10,15

161:7,17	273:19,24	early 17:12	318:15 332:17	endometriode
169:10 170:13	274:12	105:20 242:3	333:2,7 364:4	417:13
172:17 180:11	drafts 173:21	easier 164:8	390:4 412:7	endometrioid
182:23 184:3	176:24	181:24	418:15 436:6	417:13
189:8 192:25	draw 382:14	Eastern 13:14	441:13 462:10	engage 181:6
193:8,18	465:19	easy 24:18 224:5	462:25	187:2 193:18
204:25 205:2	drawing 353:16	Economic 8:6	elaborate	engaged 153:15
206:13 215:12	362:8 382:20	231:14 235:23	404:13	153:20 163:18
219:5,14	drawn 272:14	economics 94:25	elaboration	187:2 195:25
220:10 228:23	dribs 21:2	edit 158:5	211:24	196:3,5 199:1
229:10 231:11	DRINKER 5:4	168:24 181:12	electrical 186:20	410:2
232:13 233:9	drive 4:5 368:12	181:13	electron 11:17	engagements
233:19 234:8	driving 201:22	editing 162:16	427:11	136:12
234:11 255:21	313:22	162:16	electronic 165:3	engages 194:6
256:10,11,15	Drs 65:11 68:9	Edition 8:20	Elevated 10:15	England 313:8
257:4,21,22	71:18 72:5,15	290:2,19	elevates 263:13	316:23
258:20 264:9	72:16 428:23	editor 319:10	elevations	English 94:24
266:25 273:19	Drug 228:1	editorial 182:25	444:19	94:25
280:16 286:17	434:11	183:3,6 316:15	Elizabeth	enormous 341:1
290:1 296:4,6	Duces 6:13,17	469:5	312:22	ensue 315:17
304:16 310:11	due 295:15	editorialize	ELMO 45:14	entails 444:18
314:9,19	298:12	169:7	58:6 83:12	entire 18:19
317:12,13	Dulaney 2:6	edits 181:15	85:23 87:7	80:24 191:11
318:5 319:16	13:9	educating	102:8 211:2,5	221:21 246:7
320:12,12,24	duly 13:23 471:6	310:16	212:9 236:7	276:21 277:3,5
322:11 325:4	dusting 359:5	effect 271:22	271:11 291:20	293:12 343:21
326:1,20 327:3	Dusts 10:24	272:11,14	299:19 328:12	354:16
327:10 329:4	393:17	278:6 279:25	365:9 427:1	entirely 245:16
330:7,10	dying 410:18	302:12 352:19	430:22 438:2	283:1 469:18
332:10 338:20		465:9	else's 70:14	469:24
355:20 360:2	E	effective 370:8	83:23 324:7	entirety 265:8
361:2 364:14	E 3:1,1 6:1,8 7:1	effects 102:18	elucidate 286:5	entities 56:6
377:19,24	7:19 8:1 9:1	150:7 362:16	Embryology	94:11 209:14
381:15 391:2	10:1 11:1 12:1	459:17	439:6	253:22 266:7
399:13 403:14	13:1,1 294:3	effort 26:16	employ 243:24	entitled 6:23 7:8
410:17 411:8	473:2	133:11	employed	7:12,19 8:16
421:25 422:8	e-mail 164:22	efforts 182:24	238:10 243:14	9:4,15 10:4,23
426:23 427:8	311:6 444:1	256:10 306:1	461:16	11:8,12 12:4
427:15 438:24	earlier 46:23	Egli 285:8	enable 370:8	45:7 166:16
441:1 443:17	70:5 115:6	either 22:14	encompasses	214:6 281:24
443:21 444:16	179:21 197:20	46:22 55:14	125:1	328:9 364:10
444:17 465:1	202:20 259:24	92:1 161:18	endeavor	427:10
465:25 467:21	264:21 341:6	165:15 202:10	445:12	entity 33:4
470:11,13	377:25 406:13	248:16 249:19	endeavored	193:17 224:8
drabs 21:2	428:15 432:1	250:8 254:8	32:16	224:18 295:13
draft 8:11 265:3	467:25 468:12	257:21 260:2	endeavoring	entry 350:22
267:6 272:17	469:2,4	306:21 313:19	24:14	environment

8:13 364:13	244:15 252:22	346:4,6 347:8	321:6,17	190:25 194:17
406:11	265:18 288:19	348:14 350:12	349:25 357:2,2	194:22 215:24
environmental	290:2,18 322:5	374:15 375:3	359:20 362:14	226:20 238:2
94:6 97:15	381:17 383:19	375:24 386:6	373:11 375:1	239:15 254:4,6
101:8 103:6	452:6	404:20,22	379:9,14,15	254:7 263:11
149:21 150:2,7	epithelial 6:24	405:2 458:11	380:19 383:21	318:25 347:15
150:12 152:8	12:5 45:8,20	459:12 461:1	384:3 411:9	357:25 371:6
369:11,12,13	46:1 234:20	estimated 9:19	415:3,12,13,14	387:8 449:12
EOC 414:17,18	236:17 442:21	45:21 46:1	418:23 421:12	462:23 469:8
epi 78:22 94:6	epithelium	328:9 331:15	421:13 422:3	examples 41:14
144:13 425:5	439:9,10,11	451:18	424:13 435:4	exceed 350:12
454:13	Epstein 11:20	estimates 248:1	436:11 439:7,8	exceeds 346:7
epidemiologic	equipment	380:14 391:12	441:16,24	exception
10:7 11:4	186:20	et 9:14 271:17	442:9 447:24	170:12 247:9
155:7 184:22	equivalently	430:17	450:1 462:17	327:20 346:11
185:8 190:2	305:22	ethnic 236:20	463:3	Excerpt 7:6 8:19
193:21 210:22	equivocal	etiological	exacerbations	excess 352:1
238:13 239:1	221:18	285:20	371:7	466:23
245:4 262:21	era 319:14	Europe 387:8	exact 37:1,5	excesses 395:14
263:6 269:11	392:22	European 439:5	191:24 213:17	exclude 133:12
270:12,19	errata 472:4,6,9	evaluate 184:21	361:11	199:18 246:2
382:7 386:17	472:11 474:8	321:18,24	exactly 24:25	exclusion
epidemiological	error 329:10	evaluated 64:24	27:22 49:1	246:17
59:25 76:15	errors 306:1	321:25 322:1	71:21 134:12	excuse 30:5
143:25 153:16	especially	evaluating	154:9 155:13	42:17 43:15
154:1 155:11	102:13,17,21	123:2 321:5,17	208:6 296:16	50:24 96:10
211:15 264:24	108:4 239:19	322:4	308:24 319:23	120:15 159:17
381:25 397:16	322:23 403:21	evaluation	360:10 365:25	172:5 188:9
399:14	ESQUIRE 3:4,5	132:6 292:19	367:5 382:5	193:4 213:20
epidemiologist	3:12,19 4:3,9	evening 467:21	383:16	214:7 275:14
34:15 49:8	4:17,18 5:3,9	event 270:17	examination 6:2	277:14 298:11
59:14 229:17	5:16	eventually	13:25 394:1	317:12 369:23
229:20 253:19	essential 418:25	205:14	460:2 471:8	370:1 400:20
288:15 454:15	establish 446:14	everybody	examined 13:24	440:21 452:15
epidemiologists	established 32:9	57:16 175:13	examiner 27:9	executed 264:10
59:24 60:13	41:20,25	evidence 59:13	examining 8:7	exercise 91:13
190:4 317:14	226:23 227:16	59:17 89:18,23	102:20 235:24	216:10 251:2
462:3	374:16 375:4,6	210:22 211:16	example 29:16	251:10 268:25
epidemiology	376:18 394:25	212:19 214:25	48:16 60:6	344:1 347:12
8:19 11:11	404:19	216:22,25	105:19,20	359:24 455:15
55:22 77:10,15	establishes	217:5,11	106:14 118:6	exhibit 16:13,14
80:18 94:3,21	154:18	221:22 222:1	122:7 123:15	16:17 17:18,19
95:3 97:16	esteemed 317:13	234:12 236:18	156:10 157:16	17:23,25 18:14
100:21 101:9	estimate 23:7	237:7 239:16	157:19,25	18:19,24 20:4
103:2 131:25	137:13 316:9	268:11 273:3	167:21 169:23	21:14 22:3
132:7 153:3,7	316:10,17	284:19 285:5	170:17 172:17	26:2,2,12 27:1
154:23 212:18	331:17 340:20	287:1 293:13	172:19 181:17	28:24 29:12

43:6 44:20	372:19 376:12	454:5,16	367:23 371:24	eyeball 440:1
45:2 52:3,9,11	exists 81:3	461:24 468:5,9	373:20 375:19	eyes 54:21
52:21,25 54:4	294:17 344:5	469:18,23	378:6 379:11	438:15
54:7 82:7,8,9	433:5 461:16	expertise 52:15	379:13,18	
86:6,8,14 91:4	expect 38:23	52:19 57:2	380:21 383:10	F
91:4,5 95:10	225:9 359:4	78:14 96:6,8	387:21,25	F 5:18
95:13,14 98:23	expectancy	96:16 100:23	388:5 389:4	face 54:19
98:24 100:9,10	119:7	191:17 193:19	392:9 394:23	161:23 226:6
101:20 121:5	expecting 73:1	194:7 229:20	395:2 397:17	308:15
132:9 133:18	300:23	288:8	399:15 403:23	Facebook 229:2
133:20 134:8	experiencing	experts 165:15	404:3 413:9	229:6
138:16,16,18	104:1	171:12 206:3	420:1 424:14	Facsimile 11:23
138:22,23	expert 6:19 7:12	226:5 251:18	447:25 448:1	fact 14:19 15:10
139:2 213:4,7	7:16,20 21:20	255:19 256:10	450:6 456:23	35:11,14 36:5
213:9 235:17	22:10 42:5	260:23 343:8	457:5,21	41:3,23 50:12
235:18 267:7,8	51:6 55:17	410:12 430:17	458:23,24	72:12 77:16,17
281:19,23	56:1,22,23	460:2	459:9,11,19	84:14 150:9
289:20,22	57:3 60:6,12	expires 474:17	461:1,8,14,15	171:2,7 198:9
292:5 297:14	66:9,10,23	explain 274:9,10	466:8,19,22	257:2 279:1
297:17,18	67:14,21 68:8	318:23 334:13	467:4	333:21 351:25
298:3,5,22	69:12 71:4,7	374:2 385:3	exposures 369:4	356:15,21
305:6 308:6,7	75:24 76:12	explore 25:23	391:13 399:14	358:18 364:20
308:22,25	81:10 108:22	71:11 186:1	express 88:13	378:20 384:17
309:16 310:19	109:17 119:21	exploring 301:1	expressed 22:5	388:10 395:21
311:24 312:5,9	120:10 131:4,9	expose 215:10	108:3 209:13	410:2 415:21
324:17,18,24	133:24 134:9	226:13	455:4,5	420:21 432:9
325:24,24	135:23 136:15	exposed 284:3,4	extends 379:12	435:16
327:10,19,23	137:1,5 139:13	284:5 285:15	extensive 212:17	factor 126:10,15
327:24 328:5	139:24,25	286:3 331:16	316:25	214:17 225:15
351:19 366:11	140:21 145:25	340:18 366:20	extensively	262:18,23
369:16 377:16	162:3,22 168:1	386:15 389:19	370:1	263:11,16
392:25 393:1	168:18 169:17	391:8 410:22	extent 31:23	285:13 318:14
393:14 396:25	172:5 173:5	428:24 461:2	33:7 76:11	factors 7:24
397:1,4 413:23	180:16,19,23	exposure 8:16	77:13 135:17	102:12 107:14
416:18,19	181:13 183:14	10:4,11,20	136:11 137:10	125:12,18
427:4,5 431:14	184:16 185:19	11:5 46:10,13	140:24 156:7	145:6 214:6,7
431:18 437:13	186:4,24	46:14 47:4	166:2 187:11	239:20 263:9
437:19,21	187:19 191:9,9	122:21 148:23	255:8 326:12	263:18 362:17
442:19,22	202:7,25 203:8	212:21 239:16	external 54:21	362:19,22
465:20,22	205:4,7,16	263:13 270:10	64:9	factory 392:17
468:6	206:14 208:23	270:21 271:21	extra 92:24	facts 295:24
exhibits 6:10 7:3	227:25 228:5,6	277:22 278:4	extract 339:3	298:21 299:3
8:3 9:3 10:3	232:14,21	281:24 282:16	extracted	fail 472:14
11:3 12:3 70:1	233:7 256:18	283:18 284:7	327:19 336:12	fair 14:14,24
exist 337:5	257:9,20	285:12,14	351:1	18:7 20:18
344:7 461:15	264:10 327:12	286:4 364:10	extraordinary	22:2 34:8
existing 76:15	364:22 410:7	365:4,13,16	462:1	37:13 41:10

48:3 49:2	96:5 112:11	fibres 10:24	finding 163:25	firm 158:19,22
50:11 55:12	208:11 270:12	393:16 401:3,4	277:2 285:15	159:1 161:18
66:20 106:18	394:8 408:13	fibrous 399:22	353:5 362:23	173:3 206:21
107:13,20	faster 463:7	400:13,16	419:24 425:10	firms 192:9
119:5 120:8	father 403:24	field 70:14 467:2	425:11 449:19	first 13:23 19:4
121:19 124:16	fax 444:1	467:2	findings 247:14	20:4 21:14
124:20 126:7	FDA 64:10	fields 467:3	287:16 334:23	28:10 55:12,13
126:12,17,25	431:23 433:12	fifth 34:24 35:5	358:3 387:14	55:21,24 62:10
127:3,8 129:11	434:24 435:10	36:2	408:13 421:19	137:19 152:17
132:20 136:25	452:22	figure 40:6	454:21 462:22	184:15 185:6
142:10,14,18	FDA's 433:25	138:13 141:2	fine 14:3 38:20	189:25 198:11
142:22 144:17	fear 301:8 368:2	158:2 189:20	45:23 53:15,15	200:14 211:8
150:17 152:3	feature 323:6	190:3 200:24	53:19 68:6,6	212:5,13,14,15
182:16,25	features 286:12	240:8 348:1	68:22 74:10	215:1 216:19
185:5 191:19	288:12	385:3 443:10	122:17 151:14	234:16 241:24
193:19 194:10	February 21:13	443:16	156:21 166:10	242:3 274:5
197:11 201:25	21:16 22:6	figured 313:23	204:18 215:20	275:9 278:13
205:6 207:25	140:17 208:4	378:11	215:22 218:19	278:14 290:9
208:8 210:3,7	264:11 369:14	file 146:1 180:13	291:23,25	298:9 300:24
214:2 215:12	federal 134:8	393:10	292:3 300:14	302:3,10
221:18 223:21	146:1 160:20	filed 132:10	312:18 338:8	321:13 366:24
231:9 243:23	166:6	133:17	346:25 355:8	369:21 397:22
248:22 257:2	feedback 143:8	files 441:23	374:11 377:7,8	414:20 428:5
258:19 260:24	feel 73:14	filtered 250:13	400:5 428:2	444:15 463:15
268:1 270:4	221:17 320:9	Finch 4:9 6:4	440:15,15	fit 146:18
276:22 295:14	321:1 336:2	188:7,13	finish 25:2 48:11	333:15 343:20
352:7 372:10	356:12	464:25 465:2	61:13,19 62:10	fits 333:16,17
381:13,15	fees 37:24	465:21,24	62:23 113:11	381:9
382:11,15	feet 339:11	466:9,16 467:6	130:11,12,16	five 52:5 117:21
390:19,25	female 36:7,15	find 7:12 72:16	146:24 189:21	349:21 350:7,9
399:13 409:12	284:20 285:6	85:6 86:11	210:17 237:18	376:25 392:16
429:2 430:20	females 365:19	92:17 97:2	244:12 258:15	394:25
437:2,3,5	365:21,22	108:19 135:6	264:13 268:19	flashed 188:13
438:5 440:12	Ferrante 399:3	164:8 191:13	275:13,17	flat 462:25
fallacious 291:9	399:8	238:18,23	276:13 283:4	flaws 279:20
292:20	Fessler 153:9	240:15 245:3,7	303:1 330:25	flip 76:6
falls 184:9	fiber 8:17 73:23	245:10 306:10	335:5,16	flipped 67:9
false 218:4,25	74:5 90:5,13	309:14 316:12	351:20 380:11	flipping 297:3
familiar 191:11	90:19 281:24	320:16 334:24	386:19,20	FLOM 5:10
231:6 265:4	458:5,6,8	342:9 344:6	421:14 460:19	Florida 3:16
301:21 390:5	fiber/cc 391:9	347:20 371:10	466:11	flowed 270:20
390:23 459:7	457:13 458:10	375:3 376:5	finished 28:5	fluid 406:2
familiarize	458:16,18	386:16 405:25	146:25 227:10	FLW 1:5
299:23,25	fibers 72:17,22	435:9 437:6,10	227:10,14	fly 311:3
family 118:15	73:5 126:20	446:2 448:14	358:9	focus 107:18
far 37:2 58:13	127:6 401:9	448:23 451:9	finishing 235:1	149:12 201:22
58:16 92:5	457:5,21 458:7	462:4	258:14	202:2,4 205:2

356:15 379:6	82:1 88:5 90:1	219:11 220:17	374:9 375:14	239:23 243:12
focused 358:13	90:15 96:17	221:19 222:8	375:20 376:16	243:24 269:13
focuses 102:11	97:22 103:18	222:25 223:7	380:4 381:20	270:24 288:13
107:14	104:2 105:10	223:24 225:2	382:2 384:9,22	317:12 324:3
Focusing 247:15	106:6 107:16	225:17 226:2	384:25 385:15	460:9 471:5
folks 175:18	108:8,23 109:4	228:8,13	390:20 391:4	fortunately
176:12 177:6	111:11 112:5	230:19 231:3	391:19,24	227:6
194:8,9 228:17	114:4,9 115:25	231:19 232:3	396:8 399:23	forward 161:7
421:16 469:5	117:20 118:25	233:1,12 235:5	400:14 401:10	320:3
follow 42:9	119:9 120:17	236:25 243:16	402:10,18	forward-looki...
62:11,24 85:15	123:25 124:23	244:2 245:25	405:12 406:21	301:10
85:16 270:3	127:13 128:21	246:10 247:24	407:10 408:4	found 72:5,11
followed 146:2	129:9,18 130:2	248:7,17,23	408:23 409:13	72:12 89:15
following 25:21	130:25 131:5	249:11,24	410:8 411:1,13	182:13 213:20
146:11 416:7	131:11 134:21	250:6 254:17	412:19 413:14	215:4,5 222:4
follows 13:24	135:3 140:23	255:22 258:4	417:25 418:19	222:6,18
font 394:13	141:13 143:6	260:10,25	421:6 422:25	223:16,17,18
Food 228:1	143:20 144:20	262:19 263:20	423:11 428:18	242:14 244:23
434:11	145:7,16 147:8	265:20 267:19	430:7 433:13	253:13 266:17
footnotes 171:11	147:18,23	268:2,12 271:7	438:12 443:18	273:20 274:12
171:15 172:1,4	148:18,25	272:16 273:25	445:4 446:5,22	280:24,24
Ford 293:24	149:15,23	274:17 275:4	450:9,22	281:5,13
294:1,3,5,6	150:21 151:6	276:3 278:11	451:10 452:1	302:12 311:20
foregoing 471:4	152:11 155:1	281:8,15	457:1,7 458:21	314:1,3 357:8
471:20 474:3	158:14 159:13	282:21 286:10	459:4 462:10	358:2 401:3
foreign 417:17	159:23 160:12	287:6,25 289:2	463:20 464:7	419:21 424:12
forest 327:13	166:3 168:19	291:13 295:23	466:4,25	425:10,20
348:10,12	169:20 170:15	298:20 299:12	467:12 474:7	463:10,10,12
forever 112:8	171:16 172:11	301:18 304:3	formal 15:24	foundation
183:25	174:6 175:5,12	306:6 307:1,7	format 93:4	60:18 75:10
form 15:18 18:4	176:2 178:12	314:25 318:13	97:8 168:24	210:12 215:17
20:22 21:17	179:8,17	321:10,21	176:23 184:1	229:23 232:18
22:7 23:19	180:25 181:9	322:9,21 331:4	408:20 468:20	233:4 234:3
35:25 36:24	182:18 183:1,7	333:19 334:10	formatting	235:8 250:22
38:4 39:9,19	184:18 186:10	334:20 339:4	469:14	272:17 289:4,8
41:15 42:19	187:20 188:5	339:17,25	formed 242:25	290:24 291:14
43:20 47:6,22	188:11 190:22	340:6 343:18	247:23 253:16	292:2,5 295:24
49:5,21 50:25	192:4,10,17	345:22 352:3	345:20 392:6	299:3 301:19
51:19 54:14,25	193:20 194:1	352:10 353:11	399:15	310:20 319:20
55:8,16 56:2	195:5 197:13	354:4 356:25	forms 31:12	409:14 430:8
56:19 58:14	198:7,21 199:3	357:13 358:21	73:22 387:10	432:15 438:12
59:12 60:4	201:12 202:9	360:13 361:24	formula 439:12	440:16 442:2
62:4 63:24	205:10,17	362:10,25	Forrest 197:2,7	443:19
65:12 67:15	206:10,19	363:13 367:8	198:6,9	four 22:18 40:8
68:11,14 69:14	207:18 208:20	368:19 371:19	forth 21:6 39:9	349:20 350:6,7
69:20 72:8,19	209:3,9,20	372:1,5,14	131:25 145:14	fourth 369:23
73:7 74:2 75:8	215:16 218:6	373:3,17,22	205:15 239:17	Fox 398:6

fragrance 55:3 385:14	funded 294:23 311:2	142:2 146:17 182:24 207:3	give 15:16,20 23:8 29:15	195:3,4 203:21 209:23 212:8
framed 235:12	funding 148:6	213:15 235:13	37:24 92:24	213:8 216:2
framework 145:15,20 146:3,12	148:10,12,15 294:18	237:3 238:12 253:21 260:14	114:11 122:16 137:25 140:13	218:14,19 225:19 236:8
Francis 8:22	funds 148:9	262:23 263:1	152:1 162:7	244:24 266:14
frankly 26:15 257:20	further 77:25 140:4 271:21	384:24 435:11 435:15	164:13 193:6 202:19 204:10	270:5 275:6,11 275:11 292:9
fraudulent 287:14	272:10 278:5 278:17,20	generating 468:25	216:6 218:8 232:1 234:4	297:12 304:11 306:9 313:16
free 73:14 336:2 356:12	279:24 286:4,5 470:11	generic 75:4 generous 342:25	256:4 282:22 321:8 324:22	324:5 328:1,2 328:14 333:9
frequently 15:16,20 282:15	fuss 340:20 future 444:24	genital 51:17 59:3 75:7	330:14 347:14 355:15,15	334:19 335:24 338:6,7,8
friend 228:25 294:10	G	80:15,15 214:24 216:21	363:6 397:11 399:21 400:12	341:10 351:22 353:22,23
friendly 294:11	G 13:1	217:10 218:3	401:7 407:6	355:2,11,13 360:18 365:18
friends 229:2,3 229:4	gamut 107:11 GARBER 4:3	219:8 220:12 221:6 233:23	430:23 431:5,6 438:3,16,22	392:19 395:5,9 396:18 397:5
front 34:4 85:21 87:1,12 91:8	Gates 351:12 gathered 164:16	236:15 237:16 272:14 273:22	given 137:16,20 138:7 139:18	399:2 400:19 419:20 427:3
95:17 99:21,24 101:22 121:6	gathering 468:19	274:14 276:1 279:2 329:1,5	255:21 409:3 474:5	431:19 432:21 440:9 447:8
135:2 165:1 169:18 206:13	gears 280:9 GEIER 3:19	330:11,24 331:2,14	gives 295:11 343:21	463:5 464:11 464:17
208:2 210:1 227:7 247:17	general 6:20 7:17 10:22	332:19,20 333:22 334:18	giving 14:23 56:17 78:2	go-to 180:22 goal 21:24
267:12 277:16 282:3 290:5	40:17 71:24 79:7 105:2	339:10,23 344:25 347:6	105:20 207:10 234:3 283:18	251:21 343:4 344:6
304:13 324:13 352:14 355:17	107:6 133:25 141:25 147:17	genitals 333:24 genotoxic	284:7 286:3 407:21	God-given 15:25
366:14 369:19 393:15 410:10	200:17 203:10 206:15,24,25	458:20 465:5 466:1,18,23	glad 37:4 169:25 197:9	Godard 351:11 Godleski 427:16
414:7 443:6	207:13,20,20 211:25,25	467:8 gentlemen 15:25	glean 253:14 globally 215:18	428:23 goes 85:8 117:2
fruitful 445:12	212:25 223:3,8 226:22 227:15	geologist 120:6 GEREL 3:6	go 16:6 19:7 23:22 24:17	158:18,19,25 159:1 179:24
full 82:14 162:7 182:6 236:8	243:4 244:22 363:11 364:4	getting 24:7 32:10 47:3	25:22 26:20,21 39:5,8 40:5	223:23 226:11 244:21 258:13
243:8 252:19 309:15 371:20	378:5,7 379:24 389:6 411:3	70:16 113:5 114:11 130:6	44:13 45:18 48:3 58:6 63:1	258:19 284:18 285:19 291:24
469:3	447:23 456:1 General's 379:8	175:19 177:4 182:23 199:23	76:7 85:19,19 85:25 86:23	302:10 438:6 going 14:21
fully 41:20 375:1,4,6	380:19 393:4 generally 48:9	202:11 316:18 319:4 366:6	97:2 98:4 101:24 105:23	19:11 26:21 27:8,10,12
function 372:20	64:19 67:10 77:8 109:19	374:8 407:17 420:16 450:3	140:4 160:15 162:8,9 192:22	28:6,22 31:22
fundamental 205:21				

32:18 33:6,14	355:5 359:24	gotten 20:25	groups 236:20	10:1 11:1 12:1
33:17 34:1	371:10 377:10	21:9 133:14,15	guess 26:25 49:8	habit 73:24 74:3
37:23 38:8	388:12 397:10	167:22	55:20 72:20	habitual 214:23
39:3 44:1,3,16	425:24 426:17	governed 156:8	105:8 132:9	216:20 217:9
47:12 58:6	426:24 427:25	government	147:25 152:12	217:24 218:2
64:13 77:24	430:22,23	35:13	152:19 158:21	219:7,22
78:2 82:12	431:1,6,6	grab 204:16	159:4 197:18	220:11 221:5
83:4,14 85:24	435:20 438:1	gradient 362:12	205:23 211:4	hair 404:25
86:5,7,8,20	438:11,22,22	grading 392:4	246:12 264:20	406:3
89:4 92:20	439:18 440:13	grant 92:3 148:6	267:1 279:21	half 204:15
93:17 96:2	447:11 456:15	311:2 316:8,18	283:9 331:11	377:3
99:11 112:21	464:13,20	grants 148:10	349:19 350:6	halfway 45:17
112:21,22,22	469:20 470:17	148:12,15	352:17 359:10	hall 315:20
112:24,25	Golkow 13:5	320:4	359:12 360:3	hand 324:21
113:18,24	good 14:2,3,4	graph 326:2,4,4	405:14 407:1	439:23
114:17 115:10	15:23 16:11	443:8	409:15 423:16	handed 85:5
132:22 135:16	17:11 19:15	great 140:12	444:10 448:10	86:14 134:7
136:10,12	22:16 28:15	163:12 226:17	449:10 455:25	328:4
151:17 154:5	39:12 58:24	333:7 334:1,3	guessing 288:17	handwritten
154:12 156:6	65:16 68:17	343:24	guidance 33:20	334:24
158:22,23	88:20 89:12	greater 321:8	363:6	hang 216:6
162:14 166:1	100:4 124:14	349:10 389:6	guided 146:11	294:11
167:19 173:18	130:10 139:9	Green 351:11	guideline 362:8	Hank 153:9
182:13 193:6	151:9 152:4	Greenland 8:20	guideposts	haphazard
195:22,22	170:1 171:7	9:5 288:22	457:12	463:1
199:24 204:8	174:17 204:5	289:1 290:12	guts 360:11	happen 54:23
204:20 206:1	204:25 205:1	297:22 317:13	guys 21:4 185:2	93:17 181:19
212:25 215:25	223:10 227:8,8	318:1,5 320:12	226:25 306:18	319:6
216:1,1,3,13	227:8,8 230:18	Greg 403:1,2,3	313:21 377:3	happened 22:13
218:21 219:9	231:2 240:10	Gregory 1:15	397:10 413:25	316:21
221:11 226:25	241:11 252:3	2:1 6:2,12,17	430:21 431:10	happens 27:16
227:1 234:4	258:18 272:23	6:19 7:9,13,14	440:18	104:12 164:23
245:22 246:18	277:5 280:6	7:16,20 9:15	GYN 60:20,21	194:16 459:15
256:23 280:8	323:2 327:6	13:16,22 16:2	60:25 61:6	459:17
290:23 294:22	343:10 364:20	16:8 66:8	63:14 107:10	happy 39:11
299:22 304:14	377:21 391:12	100:18 133:24	gynecological	114:2 319:3
306:12 310:8	392:22 426:14	206:14 208:2	62:2 105:9	334:11 344:17
311:14,15	427:1 431:25	470:20 474:11	106:2 115:23	346:21 373:25
315:13,16	465:1 467:21	ground 320:8,25	116:6,24	hard 53:7
316:15,19	goodness 343:17	group 8:22	117:18 118:9	144:24 165:1
317:4,9 318:23	Google 242:17	152:22 190:1	gynecologist	182:5 202:19
319:5,8,17	242:20,21,21	238:25 261:10	115:20	260:11 289:14
320:2,19 326:6	244:18	261:13 309:21	Gynecology	301:6 328:13
335:23 338:5	gosh 342:8	310:14 394:9	239:5	348:1 358:24
338:14 342:20	374:12 375:15	394:20,22		358:24 433:22
342:21 347:25	GOTSHAL	395:10 396:2	H	442:16 446:14
352:20 353:1	4:19	398:20 402:5,6	H 6:8 7:1 8:1 9:1	Harlow 285:21

348:2,7,8 351:10,10 Hartge 327:22 328:6,18 329:1 329:4 330:21 332:14 333:17 333:18 335:24 336:11 338:23 339:8,21 344:3 344:4 346:12 347:5 350:6,17 351:3 Hartge's 351:15 Harvard 215:3 222:4,12 223:17 Hashtag 100:22 hazard 271:24 273:12 he'll 218:18 390:2 head 107:11 154:14 197:10 240:10 241:11 370:14 head-to-toe 105:4 headed 8:4 heading 359:1 headings 171:2 174:18 health 8:8,14 10:19 11:21 46:21,25 47:18 47:20 48:6,15 48:23,25 94:7 95:2,6 100:22 101:21 102:1 103:7 107:14 231:15 235:24 260:18 264:21 265:17 266:5 266:11 267:6 267:14 268:10 272:13 273:20 274:12 275:24 278:10,25	367:15 369:24 370:3 378:6 409:3,10,20,23 432:2,8 healthcare 144:9 462:3 hear 15:14 115:6,8 220:7 260:6 307:22 321:12 348:24 466:14 heard 116:9 154:4 202:20 227:4 258:3 294:22 307:15 330:6 354:21 389:16 406:25 409:20 410:15 hearing 6:21 7:18 8:7 70:24 71:13 133:25 202:11 206:16 207:17 231:14 232:11 233:20 236:6 332:11 heart 107:9 HEASLIP 4:18 85:12 464:17 heavy 387:21,24 395:1 heck 360:16 held 2:1 13:8 338:15 377:15 440:24 464:21 467:18 Heller 273:2,5 280:17,18 281:23 282:6 428:14 help 27:4 122:2 133:11 157:24 158:1,5 162:15 168:18 172:19 175:3 176:1 180:7,15,23 185:19 186:3 186:23 193:12	193:25 197:9 301:10 410:11 410:11 helped 20:12,16 91:18 168:23 169:11,12 170:24 311:2 helpful 164:7,9 303:13 helping 468:20 helps 155:9 172:19 340:23 Henderson 285:9 hey 112:20,20 431:10,10,10 Hi 467:22 high 41:8,8 269:17 289:21 380:15 406:2 higher 155:25 215:9 226:13 226:22 282:15 347:10 354:3 367:21 highlight 70:10 highlighted 31:4 70:5 highlights 30:18 30:23 69:22,24 highly 36:2,3,16 37:20 256:13 Hill 145:6,10,15 145:23 146:2 146:11,19,20 147:5,14 239:11,21,24 268:11,15,23 269:9,16 270:14 271:1,4 271:18 278:1 358:24 362:22 419:8 Hill's 447:22 hired 224:11 histologic 422:2 histology 417:13	historic 391:13 history 282:16 283:19 284:7 285:16 286:4 hold 24:10,10 28:21 44:2 98:5 120:9 144:1 236:19 314:9 323:9 366:6 438:19 438:23 439:17 439:24 holds 100:20 holler 88:24 Holmstock 5:23 13:4 home 30:11 404:13,22 456:25 homes 102:17 honestly 55:19 73:18 88:9 96:19 133:1 230:3,21 429:3 hope 38:6 113:20,20 198:22 205:18 207:8 352:19 434:22 446:18 hopefully 205:4 hoping 133:16 314:21 Hopkins 7:11 9:7 15:6 34:19 48:7 93:19 95:9,21,24 96:21 98:4 100:8,19,21 104:9,25 118:20 205:9 208:9,14,19 209:1,17 213:21 223:14 224:6,7,22 225:10 230:2 294:7 308:15 309:20 310:2	310:13 312:2 313:7,8,9,10 313:24 314:2 Hopkins' 309:13 hospital 9:17 96:1,3 117:4 224:17 325:12 345:5,5,17 hospital-based 356:8,15,21 357:3 358:14 359:14 360:8 hospitals 345:12 Hotel 2:5 13:9 15:2 hour 23:14,24 24:19 177:18 177:22 204:16 377:2 hourly 23:10 24:2,6,21 178:20 hours 23:4,8,8 25:17 257:13 257:13 376:25 467:13 house 231:12 404:16 household 10:14 284:5 369:4,8 huge 387:20 human 10:25 11:21 285:7 439:4,5 448:14 448:22 humans 449:13 humongous 379:2 hundred 14:13 14:15 155:22 155:23 301:22 344:15 453:23 458:13 hung 199:24 hurry 463:6 Hutfish 4:20 hybrid 291:15
--	---	--	--	--

hygienist 120:1	346:10	405:11	include 47:2	360:6 463:12
hypothesis	identification	impacts 84:7	100:23 101:6,8	incorrect 121:12
89:19,23	16:15 17:20	97:15 101:9	107:2,5 120:14	155:2 179:16
315:11 316:11	18:25 44:21	149:21 150:2	120:15,20	increase 102:22
420:1,10 439:8	52:12 82:10	150:13	122:7 123:5,7	108:5 214:24
441:17,25	91:6 95:15	impenetrable	133:12 146:17	216:21 217:2,3
hypothetical	98:25 133:21	181:22	245:17 247:1,8	217:10 218:3
78:21 79:3,22	138:24 213:10	imperative	247:9 251:3,21	219:8,24 220:1
80:18 234:4	235:19 267:9	46:21 369:24	252:25 339:15	220:12 221:6,9
235:7 383:7	281:20 289:23	370:3 472:10	355:1 363:21	221:9,10,14,15
hysterectomy	297:15,19	implemented	388:17	221:16 237:21
285:16	308:8 312:10	367:15	included 43:23	371:6 379:17
I	324:19 327:25	implementing	146:5 225:14	380:20 402:1
IARC 10:23	366:12 369:17	292:11 368:1	245:2,9,9	417:15 420:3
41:21 239:3	377:17 393:2	implicated	246:20 249:3	increased 215:5
241:11 252:18	397:2 413:24	285:20	251:12 264:23	222:6,18
253:12 259:2,5	416:20 427:6	implication	268:4 336:19	223:19 233:22
259:6 260:4,8	431:15 437:20	160:10 405:18	includes 95:25	234:14 236:16
260:18,21	442:23	implications	101:3 107:22	237:17 384:19
261:8,12,21	identified 36:21	363:8	305:23 332:21	389:5 413:11
262:16 387:3,5	134:6 241:12	implied 405:24	354:12,20,23	414:17 422:23
387:5 391:16	identify 238:12	importance	355:4 401:4	423:9
391:22 392:6	246:16 247:22	303:25 304:22	including	increment 371:7
392:12,12,14	350:11 353:22	important 41:7	102:16 237:23	increments
393:17 396:2	354:2 438:4	53:17 254:6	252:6 310:14	371:14
397:15 398:20	identifying	293:11 315:4	349:24 467:5	independent
399:16 400:19	102:11 172:22	323:16 342:10	inclusion 217:4	153:21 154:8
400:20,25	ignore 246:18	342:13 360:15	245:24	154:16 155:15
402:4 412:4	322:13	387:20 403:4,9	inclusive 251:7	251:2
457:16	II 226:19 392:22	419:2 451:17	251:9,9	indicated
IARC's 392:7	iii 276:15	451:19	incomplete 46:7	165:17 254:14
399:16	ill 105:14	impossible	78:21 79:2,21	315:4 398:22
ICTR 310:25	illness 117:8	85:15 90:16	97:24 98:21	403:4
ICTRs 294:22	319:25	impressed	235:7 383:6	indicates 19:5
ICU 105:22	illnesses 104:15	185:22,25	414:21	379:14,15
143:13	370:22	218:18	inconsistencies	380:20
idea 194:25	imaginable	improper 83:22	359:6	indicating
230:3 284:12	117:8	193:5 455:21	inconsistency	465:17
317:15 323:5	imagine 104:12	456:17	286:22 287:1	indicative
336:4 382:20	352:12,14	imprudent	356:19 358:2	271:22 272:10
429:3	383:24	79:18 80:12	358:20,21	277:19 278:5
ideal 332:18	Imerys 109:25	87:18	359:9 360:1	278:17,21
333:1 340:21	110:5 442:2	inappropriate	inconsistent	279:25
344:19 394:18	impact 150:6	160:17 161:1,5	291:6 292:14	indicator 323:24
ideas 301:5	342:24 383:19	incessant 115:14	293:9 355:23	403:25 404:2
identical 213:22	384:19 385:22	incidence 46:22	356:1,14,16	406:8
	impacted	389:19	357:9,24 360:5	indisputable

433:9,17 435:3 individual 193:17 244:19 individuals 47:4 47:19 60:14 75:6 106:20 215:14 232:15 284:10 309:23 409:4 indoor 368:25 369:25 370:4 370:18,25 371:17,24 372:12,23 373:15,21 374:7,17,23 375:19 376:10 induce 420:2,10 induces 423:19 industrial 119:25 387:21 387:25 industry 232:11 infected 383:2 infer 283:13 379:10 inference 298:17 362:8 inflammation 12:5 102:19 126:3 241:18 241:20 413:8 418:6 420:3,9 420:24 421:4 422:3,5,12,23 423:9,14,17,20 424:14 425:21 439:10 442:21 443:11 444:18 444:21 inflammatory 107:9 417:19 420:1,23 432:11 inform 71:23 363:15 407:24 408:12 409:10	440:4 information 9:12 16:24 22:17 47:3 56:18 57:12 59:25 71:6 75:16 91:16 98:17,19 102:1 162:21 164:22 165:24 166:17 167:1,2 172:1 172:2,10 175:23 224:25 225:7,15 237:6 237:22 238:1,5 239:6 248:21 249:2 253:14 253:22 266:12 266:17 272:22 279:20 322:12 336:20 339:9 341:2 342:6 343:21 344:18 357:15 363:5 386:2 392:8 434:8,18,25 441:11 445:21 451:2,2,3,4 456:11 457:10 457:17 460:17 informative 456:14 informed 30:8 30:10 59:2 informing 251:17 informs 270:13 ingested 266:21 Ingham 26:12 26:13 27:19,25 29:13 55:9 133:12 138:1,4 138:7 141:4,7 197:1,7,12 199:18 Ingredients 55:3 inhalable	102:23 108:6 inhalation 54:19 57:4,22 201:13 413:10 414:15 415:4,8,10,11 inhale 142:4 405:7,16 inhaled 266:22 405:19 406:1 415:15,22 457:5,22 initial 279:16 initially 250:12 initials 216:3 initiates 439:10 inner 48:18 102:17 Inner-City 10:17 innovative 301:9 inpatient 105:14 input 183:17 198:1 272:22 inputs 368:10 inquired 232:5 inquiry 31:16 insert 182:2 insignificant 287:19 insist 183:16 instance 194:6 264:1 instigate 417:18 418:6 Institute 9:7 294:13 308:16 313:9 institution 225:1 instruct 135:17 136:12 173:19 176:15,19 instructing 156:19 166:5 177:9 218:11 instruction 166:11 167:4	INSTRUCTI... 472:1 intellectual 183:17 intelligent 329:24 intend 399:21 400:12 401:7 408:15,18,21 intending 401:20 intensive 63:6 104:10 105:8 105:11,13 intent 198:23 intention 92:22 408:16 intentionally 274:2 330:4 332:7 420:14 interest 107:21 108:3 196:15 196:23 200:3 314:23 315:1,3 322:14 349:4 374:5 interested 102:13 108:1 150:10 153:6 155:6 163:19 185:8 195:10 332:11 342:9 448:2 interesting 150:3 311:17 313:18,20 315:18 347:21 interests 97:14 97:21 101:8,15 103:2,12 143:1 interfaced 174:21 interject 31:23 166:2 internal 34:21 64:9 94:18 105:2 107:7	International 10:8 45:9 364:12 internist 118:16 interpret 77:18 287:16 373:25 386:22 454:20 interpreted 239:6 323:16 interpreting 198:2 318:16 interrupt 39:1 243:17 interruption 251:24 intersection 465:10 intersects 458:20 459:3 466:2,20 467:9 interstitial 122:9,11 interval 305:23 328:19 329:7 330:12 353:10 354:3,10,11,16 355:3 intervals 317:2 327:18 353:8 357:9 intervention 370:8 intrapерitoneal 285:14 introduce 15:24 introduced 152:17 introduction 413:17 454:20 invent 344:9 inverse 463:11 investigating 234:9 investigation 294:7 invite 261:5,5,12 261:21
--	--	--	---	--

232:15 261:7 invites 260:22 invoice 23:1,5 24:20 34:5 158:24 161:14 161:24 invoices 22:18 22:21,25 40:4 40:8 158:4,13 179:2,12 468:25 involuntary 10:20 378:6 393:8 involve 33:8 157:17 involved 60:20 67:18 128:3,6 128:9 144:23 147:16 152:9 152:12 163:13 194:21 200:21 209:12 230:8,9 240:6 248:12 319:24 428:15 involving 199:11 254:16 365:12 IOM 394:2 irregularities 256:12 issue 9:10 41:19 47:20 79:7 81:4 129:25 135:18 142:11 142:16,20 150:19 166:8 199:2 225:4 241:10 246:23 251:23 261:14 294:18 298:16 299:5 301:2,8 308:18 309:3,9 337:8 359:2 387:15 391:16 394:14 448:7 449:1 467:10	issue's 309:9 issued 264:22 295:18 issues 25:1 57:4 134:10 145:22 254:16 256:22 257:17 462:12 item 66:9 67:19 150:25 items 20:19 22:3 22:4 iterative 91:13 238:19 Iturralde 285:10 <hr/> J J&J 19:16 157:3 159:16 184:15 184:25 185:1,2 210:9 441:22 J&J's 27:7 JAMA 328:6 Jersey 1:2 3:22 4:21 13:15 JESSICA 5:9 JJCI 53:17 JNJ 8:18 9:22 job 55:20 93:15 93:15 132:21 191:18 jobs 215:9 226:13 Johns 7:11 9:7 15:6 34:19 48:7 93:19 95:9,20,24 98:4 100:8,19 100:21 118:20 205:9 208:9,14 208:19,25 209:17 213:21 223:13 224:6,7 224:22 225:9 294:7 308:15 309:13,20 310:1 313:10	Johnson 1:4,4 4:16,16 13:11 13:11 49:17,18 49:19 50:1,1 50:12,13,19 51:6,6,7,15 53:4,12,25 55:6,6,14,14 55:17,18,25,25 56:5,6,13,13 57:10,10,20,20 63:22,22 64:4 64:4,23,24 65:3,3 69:11 72:17 74:11,11 74:21,21 75:15 75:15 78:3,10 78:16 79:17,19 79:19 80:8,13 80:13 81:13,13 81:17,17 84:10 84:10,16 87:17 87:19,19,23,24 108:22,22 109:3,3,7,8,16 109:16 136:8,9 136:16,16 137:1,1 150:18 150:18 151:3,3 157:9,9,12,13 157:17,18 158:10,10,20 158:21,24,24 158:25 159:1 161:19,19 165:16,16 381:17,17,17 381:18,18 382:24,25 384:23,23 385:12,12 406:15,15,16 406:16 407:2,3 407:6,6,19,19 407:22,22 Johnson's 7:4 49:19 50:19	51:7,15 52:8 53:4,13,13,21 53:25 54:1 56:16 69:11 72:18 74:15 78:3,9,10,17 79:17 80:9 84:16 87:17 joined 312:7 joint 100:20 Jonathan 185:11,12,13 185:17 186:22 194:22 195:3,4 195:12 Jordan 347:16 journal 10:8 45:9 123:21 125:18 126:13 127:9 144:18 145:14 147:6 299:5 315:13 364:12 369:10 411:10 439:4,5 Journal's 316:23 journals 121:16 judge 39:10 71:5 113:21 114:2 218:15,17 219:4,4 220:9 220:14 337:16 337:23 338:9 judgment 251:3 251:10 336:13 361:19 362:14 July 71:5,17 219:6 jumbled 202:12 jump 132:22 156:6 June 92:6,10 121:9,13 jury 16:1,3 70:17,23 205:15	K K 3:5,7 KATHERINE 5:3 keep 27:11 53:14 54:18 85:23 112:7 164:14 168:12 177:13 242:9,9 334:7 358:25 451:11 Ken 287:21 288:7 290:9 kept 347:5 key 241:12 keywords 268:24 Kim 364:9,14 Kimmel 7:22 214:3 215:14 224:24 225:5 225:12 228:17 kind 29:24 46:10 56:21 57:12 63:8 70:11 74:2 97:2 104:7,11 104:18,24 105:4 154:19 181:15 195:2,7 212:2 240:19 242:10 254:7,8 257:10 266:7 269:7 289:1,11 299:14 333:22 333:25 336:16 341:21 348:12 402:24 404:5 406:17 421:19 450:1 452:25 kinds 64:17 97:7 126:3 162:11 209:13 224:14 224:15 266:19 342:24,24 358:3 412:8
---	--	---	--	---

421:7 448:20	144:12,13	235:9,10,11	320:2,8 321:4	451:3,14,15
knew 153:1	147:10 149:2,4	237:2,18,20	321:23 322:1	452:5,12,23,24
155:8 185:20	153:19,24	238:2,19,22,23	322:11,12,14	454:14,25
186:6 312:3	155:19 157:5,6	239:3,13,22	323:8,11,12,14	455:8,10 457:2
383:9,14	157:13,15	240:4,6,14,17	326:11,22	457:11,15
435:10	158:2,5,17,18	245:19 247:12	329:25 331:9	458:10,12,14
know 14:15,21	158:19,22,25	250:14,15	331:24 332:16	458:15 459:15
15:12,15,19,20	159:24 160:4	252:5,11 253:8	333:1,4,20	461:21,22,25
21:4,21 24:7	161:12,19	255:5 256:21	334:5,13	463:6,14
25:21 26:23	162:13 163:8	259:25 260:12	336:11 337:4	466:13 467:1
29:5,16,23	165:2 168:5,21	260:14 261:3	340:15,19	468:19,21,21
32:25 35:2,3	169:21,25	262:2 263:10	341:7,20	468:22,24
35:13 36:13,16	170:20 171:3,6	264:18,25	342:19 344:19	knowing 163:20
36:19 37:3,8	171:24 172:20	265:11,22	348:2 349:13	289:18 388:10
37:21 41:6,10	174:18 175:20	266:3,4,5,6,10	353:3 358:19	knowingly
44:8 46:3,4,16	175:22,23,25	266:13,18	359:6,13,16	304:9
48:2,13,14,17	176:7,8 178:14	268:21,21	361:6,13,13,14	knowledge
48:22,25 49:7	178:15,23	269:10,19,19	361:15,20,20	40:20 255:11
49:14 50:8,16	182:7,10	270:14,22	363:4 364:15	known 110:14
51:11,20,21	183:19 185:16	272:21 276:23	367:19 368:6,9	152:13 186:8
53:9,18 58:16	186:14,14	279:22 281:4	368:11 369:6	215:7 225:24
63:4,11 64:18	187:22,23	281:16,17	371:16 372:22	226:9 284:8
67:3,7 68:5,23	190:1,23,24,25	283:11,13	374:4,22,22	373:4,6,7
69:2,5 70:2,9	190:25 193:2	284:11,13,13	375:13,17,17	455:15 459:17
70:11 72:12,20	194:16 195:6	287:14,14,21	376:11,23	knows 15:12
73:22,24 75:12	195:19 196:11	287:22,22	379:2 382:8,9	133:16 313:18
79:23 81:6,14	196:16,17,19	288:1,3,7,12	387:6,14 388:4	Kotsopoulos
82:4 83:3 88:9	196:19,22	288:20,21,23	388:8,20,22	351:13
88:23 90:5	197:19,21,24	288:24,24,25	389:17 390:4,5	Kurta 351:13
91:15,15 94:9	198:1,2,9,12	289:6,9,11,14	391:12 392:23	
95:23,23 96:19	200:21 206:1,2	293:16,24	401:19,25	<hr/> L <hr/>
97:6,8,9,11,11	206:2,9,20	294:4,6,17	403:5 405:15	L 4:3
97:24 100:4	207:21,22	295:9,12,12	405:17,22	label 94:10
104:6 106:9	208:11 210:8	296:1 299:6	408:1,10,13	95:24 314:13
107:6,10 109:1	212:23 213:18	302:22 303:4	409:16,19,22	labeled 239:10
109:7 110:5,8	213:19,21,21	303:10,10,20	412:9 421:16	353:19
110:21 113:7,8	216:12 217:19	303:20 306:17	421:17 422:2	lack 286:19
115:5,10	219:19,25	306:20 307:23	424:10,19,25	304:1,23 405:5
116:22 117:5	220:23 222:15	308:24 311:4	425:5 426:6	460:25
118:2,7 119:22	224:6,7,8,9,10	311:18,20	429:9,12,12,13	lacks 60:17
123:2,5,16,17	224:10,14,17	312:22,24,25	433:15,16,23	75:10 210:11
125:2,22 126:1	225:5,7,8,8,10	313:2,3,5,18	435:8,12 437:7	215:17 229:22
130:8 131:8,19	226:16,18	314:3,12	442:6,6,7	232:17 234:2
132:16 133:8	228:23 229:10	315:14,15,16	445:7 446:24	235:8 250:21
137:12 140:24	229:17,18,24	315:17 317:3	447:4,5,23	272:17 295:23
141:3 142:7	230:21,25	317:11,19	448:19 449:12	299:2 301:18
143:8,10,13	231:5 232:19	318:4,4,5,5,6	450:11,19	409:13 430:7

432:14 442:2 443:18 ladies 15:25 112:20 laid 292:5 Langseth 425:13,14,20 language 225:14 226:16 279:5 392:2 large 86:11 123:3 361:13 361:14,14 larger 305:21 362:17 Lash 8:21 289:7 289:12 290:14 late 39:17 40:14 407:17 lately 229:25 latency 41:10,13 41:24 45:19,25 46:8,9 latest 455:3 462:22 latters 239:19 laughed 353:2 law 158:19,22 159:1 161:18 173:2 192:9 206:21 lawsuit 109:15 lawsuits 184:17 lawyer 185:7,10 194:12 lawyer's 18:5 lawyers 18:14 184:25 195:2 209:5,7,10,12 276:24 lay 290:24 Lazar 309:8 lead 126:4 302:20 309:4 369:8 370:11 370:12 413:11 421:18 423:20	427:15 448:1 leading 415:15 leads 439:10 learned 152:22 317:10,10 leave 93:10 185:2 237:10 256:9 384:12 leaves 217:2 leaving 237:5,12 237:22 lecturing 301:4 led 283:12 383:10 leeway 268:21 left 21:25 182:8 254:21 291:17 293:16 320:24 406:6 left-hand 45:18 444:16 legal 71:22 109:10,17 131:4,9 134:20 134:25 137:1 188:2 193:19 202:7 207:3 228:5 428:9 legitimate 270:25 legs 339:11 Leslie 1:25 2:16 13:20 471:18 let's 18:11,14 23:7 25:2 27:11,15 41:13 44:11,12 45:14 47:20 83:20 85:22,23 100:7 100:12 101:17 102:7 121:1 122:14 133:18 158:7 161:14 170:10 184:14 192:20 209:23 210:24 218:19 218:20 225:19	231:10 236:8 243:21 263:8 263:15 267:5 275:11 297:12 297:16 298:9 299:18 305:5 305:18 320:15 320:17 324:2 338:8 353:24 355:11,13,14 358:10 360:18 360:19 374:20 376:21 396:18 398:13,17 399:2,20 416:17 431:12 431:13 447:8 464:11 letter 11:20 431:23 441:2 443:16,17 level 272:20 284:9 387:24 406:2 456:23 457:4,21 459:16 466:22 LEVIN 3:13 LHG 1:5 Liability 1:7 13:12 life 119:6 203:10 lifetime 379:11 420:22 lifted 115:7 ligation 285:17 light 11:16 427:10 limit 52:18 97:9 limitation 421:18 limitations 460:9 limited 39:18 40:15 395:21 line 9:18 55:2 80:16,24 83:11 84:2 87:11	97:13 214:12 266:16 349:18 350:10 353:17 361:9 369:22 369:23 473:4 lines 436:1 452:12,14 link 172:24 240:14 372:2 386:13 422:5 linkable 404:3 links 386:16 389:11 list 20:20 21:8 21:14 35:12,14 43:2,7,9,10 65:21 67:21 138:13 139:12 139:16,22 157:20 162:8 165:18 182:6 182:11 188:16 244:6,18,20 247:1,25 248:10,13,15 248:20 249:12 249:19 252:19 253:11 269:11 312:6,15,16 313:4 316:25 364:19 388:15 388:19 468:23 469:3 listed 20:19 22:3 35:1 65:17 142:23 146:9 165:7 180:14 188:1 214:17 238:20 244:9 246:6 250:7 251:15 252:20 267:20,21 325:5 326:1 328:17 332:14 333:10 334:16 388:17,18 listen 39:4,21	106:24 113:5 194:13 329:22 469:21 listening 345:10 listing 268:23 lists 35:2 42:15 238:21 325:25 327:12 literally 26:25 27:21 34:20 93:14 107:24 119:2 123:14 172:21 183:21 206:21 208:12 213:16,22 216:14 217:15 230:23 273:8 279:16 298:15 313:6 332:20 355:24 456:14 458:24 459:18 459:19 literature 35:24 39:16 76:16 79:10,15 121:11,21 124:5 126:8,18 148:22 162:20 163:5,23 164:3 164:11 184:22 185:9 212:19 222:21,23 240:2 242:2,7 242:25 245:1 246:5,7 264:25 271:24 291:4,5 291:6 292:13 373:14 374:6 375:7 382:7 386:17 389:1 407:6,20 409:9 411:22 412:16 416:4 422:9,22 423:3,7 441:15 448:5 451:21 453:15 454:13 461:17 462:15
---	--	--	--	--

464:2	232:16 234:1	66:6,10,13,24	392:19 397:22	97:1 171:8
litigation 1:8	235:6 248:24	68:9 69:10	416:16 419:13	201:22 266:2
13:5,13 56:7	261:1 265:1	70:25 71:7,18	428:5 430:22	266:11,15
67:19 129:14	271:6 274:16	72:5,15,16	431:22 438:20	268:3 306:15
129:17 130:3,4	291:12 293:1	Longo's 67:4,14	440:1 443:10	317:25 348:5
130:20 162:4	295:22 298:19	70:18	443:15 449:10	349:18 380:5
180:20 407:7	302:18 304:24	look 20:17 29:7	454:13,24	443:23 449:23
407:21 409:21	306:7 307:2	30:13 37:4	462:4 469:7,10	465:16
410:3 439:1	325:8,15,17,21	41:7 52:22	looked 26:7	loose 46:15
little 24:24	348:21,24	54:10 56:15	50:18 51:7,12	lost 166:22
29:20 30:12	364:2 367:18	69:16 87:6	65:10 67:8	lot 21:2 62:6
46:15,15 54:11	368:7 380:23	96:3,5,21,25	69:4,6 182:15	70:7,9,10
54:12 59:15,21	381:8 382:3	100:7 102:3	213:22 226:20	99:23 168:22
73:12 77:25	385:25 391:25	121:17 123:1	239:8 241:13	169:2 200:25
115:6 121:1	402:9 406:20	138:12 141:2	242:16 245:18	207:22 224:4
152:2 158:7	407:9 408:3	143:9 144:21	252:17,18,20	237:6 302:19
186:1 205:3	410:25 411:14	147:12 149:3	253:2 266:19	310:21 315:6
230:11 238:7	411:25 412:21	153:25 161:14	268:7 282:23	332:22 341:2
241:23 245:12	413:13 414:25	168:16 171:1,6	312:1 336:13	360:16 403:7
279:10 343:20	416:1 417:24	171:10 173:17	344:10 374:23	418:2 423:6
343:21 352:24	418:20 420:12	174:11,16,17	391:16 398:21	435:21 449:22
355:6 360:19	422:16 423:24	176:9 179:1	409:16 421:16	452:12,14,16
371:14 376:21	424:17 429:10	181:17 182:21	433:18 435:22	452:21 460:7
377:2,24	430:6,10,15,19	183:21,25	436:18 448:6	lots 387:10
399:20 400:3	431:5 432:4,13	196:16 213:13	448:13,21	415:2 451:2
407:16 423:6	434:15 435:7	222:22 226:18	452:3 457:15	loud 115:9
463:7 468:12	436:16 440:6,9	238:21 251:20	457:16	lousy 47:9,15
live 315:9 317:7	445:3,16 446:4	252:23 254:6	looking 28:8,10	low 93:3 149:10
318:18	446:21 449:6	257:18 267:15	28:16 104:4	269:17 446:15
living 287:24	450:10,23	267:19 272:24	130:21 153:2	459:15
315:10,24	452:2 453:6,21	272:24 277:14	172:14 211:7	lower 319:12
374:21 380:22	457:8,24 464:6	290:5 293:14	213:23 239:13	343:15 419:13
LLC 4:10	467:11	301:25 303:23	239:23 242:11	419:20
LLP 3:6 4:19	Logan 5:5	308:11,25	252:22,25	luck 319:4
5:4,10,17	long 24:9 39:5	313:16 316:22	283:17 293:12	lucky 105:1
local 190:3	82:17 83:2	323:6,7 327:21	297:4 301:22	lump 383:1
location 379:13	93:16 117:9	328:22,25	316:9 323:14	lumping 197:20
locations 104:9	152:9 170:11	329:13 337:6	323:15,15	lunch 204:6,21
LOCKE 5:16	174:24 181:22	340:16 341:10	340:13 346:3	lung 11:6 97:15
73:6 88:6	268:18 300:6	341:10 342:1	355:20 356:3	100:24 101:9
89:25 110:18	300:15 329:13	342:25 344:17	365:10 366:18	103:3 106:20
118:12 145:8	341:12 440:3	345:11 347:16	371:10 376:9	122:7,8,10,11
186:12 191:20	469:8	353:8 355:24	390:9 409:17	122:18,20,24
192:3 200:9	long-term 59:10	356:12 359:24	428:24 463:2	123:2,5,7,13
202:1 217:12	longer 39:5	365:2 369:21	looks 20:13 21:2	123:14,18,19
218:5 220:16	94:12 420:2	371:4,5 378:17	29:25 37:4	123:23 126:5
223:25 231:18	Longo 65:11	378:21 387:3	54:12 92:5	143:1,5 150:7

202:23 284:10	45:25	369:16 377:17	168:15 180:4	64:9,16 69:21
364:1 365:4,16	malpractice	392:25 393:1	284:20 285:6	70:11,11,24
368:3 372:3,3	203:18	393:13 396:25	285:12 368:25	73:21 75:19
372:12,16,18	man 329:24	397:1 413:23	370:5,18 371:8	77:6,8 79:24
372:20 376:11	management	416:19 426:24	371:25 372:12	82:22 88:9
376:14 378:1	123:18	427:5 431:14	372:23 374:8	91:13 96:20
379:11,17	MANGES 4:19	431:17 437:13	374:17,25	106:9 107:6,10
380:3,21	manner 47:20	437:19 438:8	375:19 376:6	108:19 112:8
397:18 398:1,2	161:4 409:11	442:18,22	376:10 404:19	118:17 126:22
398:11,15,24	Manuscript	468:6	404:21 458:8	131:23 132:15
399:11 404:3	10:13	markers 423:14	matters 69:2	136:19 142:8
414:15 456:25	Maple 3:21	Marketing 1:6	158:20 168:14	143:15 144:22
lungs 90:18	March 8:10	13:12	266:23 450:25	144:23 145:19
371:24 415:18	231:12 236:1	marketplace	Mc 8:5	146:16 147:13
Luzenac 11:24	296:19 297:23	75:5	MCBETH 5:3	147:25 149:17
438:10	298:15 305:10	marking 26:13	McCormack	150:24 153:20
Lv 366:1,15	308:19	70:1	369:3,8	155:25 158:21
lymph 11:19	mark 16:12	markings 30:14	McDonald	162:24 163:25
123:3 412:17	18:14 66:11,24	30:17	427:15 428:23	163:25 164:7
412:25 427:12	69:19 86:5	Maryland 1:16	McShane 9:6	164:14 168:22
428:9 429:8,20	91:2 355:7	2:7,18 13:10	318:1	169:12,14,22
430:4	465:21	15:2	McTiernan	170:5,25
M	marked 16:14	masses 123:2	232:13 233:9	171:25 172:10
M 3:19 4:17,18	17:17,19 18:12	matches 406:10	233:19 234:8	172:20 174:16
M.D 1:15 2:1	18:24 26:12	matching 85:4	234:11 235:22	175:20,20
6:2,17 7:7,13	28:23 44:20	material 18:22	MD 6:12,19	176:5 179:20
13:22 470:20	45:2 52:3,9,11	159:8 242:10	7:10,14,16,21	180:7 182:5,8
474:11	52:25 54:3	242:11	9:16 206:15	187:4 191:23
machine 405:22	82:7,9 91:4,5	materials 6:21	MDL 1:4 13:13	195:1,8,17,20
Maddie 174:22	95:9,14 98:23	18:3 19:5 20:5	38:2 55:9	196:12,19
174:25	98:24 132:8,9	20:6,19,25	111:3 131:10	197:8 198:12
Magnani 398:18	133:18,20	21:7 23:17	135:1 199:20	198:22 199:16
398:23	138:14,15,17	34:10 42:5,15	MEAGHER	199:19 201:16
main 174:22	138:22,23	65:17 66:2,8	5:10	202:20 203:9
240:23 242:21	213:4,7,9	111:15 112:10	mean 15:13	203:18 205:18
252:21,21	235:17,18	153:24 157:19	20:10,25 21:19	205:21 208:11
mainstream	267:5,7,8	157:20 159:19	21:23 27:1	209:4,11
306:19	281:19,22	468:19	29:6 34:9,10	211:24 215:19
majority 142:23	289:20,22	maternity 93:10	35:3,3,11,11	216:11 217:16
245:20 286:3	296:18,18,23	matter 10:16	35:12 37:1	221:22 224:21
making 28:8	297:13,14,16	13:10 21:1	40:5,24 41:21	225:5 230:22
44:8 115:14	297:18 298:10	27:25 60:7	46:10 47:25	237:5 241:22
234:6 301:7	308:5,7 309:15	67:7 68:25	48:9,14,14	242:13 243:17
303:14 368:4	311:24 312:5,9	102:14 103:7	49:11 50:16	244:8 245:3
469:11	324:15,17,18	120:11 124:18	51:22 52:18	249:15 252:7
malignant 45:20	327:22,24	134:9 163:10	55:9,9,20	253:7 258:7,7
	328:4 366:11	167:9,16	56:22 60:8	260:1 263:1,4

264:15,17	466:6 467:15	446:1,12,13,20	medicine 7:11	142:16,20
265:11 267:16	meaning 28:13	446:25 447:6	34:18,21,22	148:10 201:25
267:18 268:14	104:9 131:23	449:18 450:8	52:16 57:3	207:10 263:8,9
268:24 270:11	133:11 144:13	450:19 451:8	61:1 63:17	395:12,22
272:24 273:15	201:17 238:19	451:23 453:4	93:4,20,23,25	397:19 457:22
281:16 294:11	239:19 266:18	455:2	94:6,18,19	458:5
295:10 301:20	457:11 462:25	mechanisms	95:9,24 96:11	mess 269:7
302:20,20	466:21	422:10 449:2	96:12 98:5	463:3
303:6 310:21	means 49:14	453:4,19 455:6	100:18,19	met 189:25
311:11,14,15	81:23 82:5	medical 15:6	105:2,5 107:7	465:2
313:12 315:8	119:22 169:2	24:19 25:18	143:5 189:1	meta-analyses
318:22 320:1	185:3 187:24	30:4,5,10	201:10,19	238:20 240:11
321:24 323:1,2	321:24 372:17	31:11,17,21,25	205:9 294:8	244:19 251:16
323:7 329:17	405:16 456:1	32:6,11,14	Medline 242:17	267:17,25
333:2,14,20,22	466:8,22	33:3,4,19 34:1	244:17	268:8 368:22
334:2,11 336:5	471:22	37:11 39:16	meeting 157:23	meta-analysis
340:20 341:1	meant 64:16	56:13,18 57:12	meetings 260:21	10:6,12 11:14
342:8,20 343:2	130:19 256:19	81:12,16 95:21	261:23	245:21 246:7
343:19 344:6,9	259:15,16	95:22,25 96:3	member 94:20	265:12 266:25
344:18 346:20	308:12 345:13	96:4 100:8	295:3,6	271:16 277:25
352:17,18,23	388:17,20	104:7,11	members	364:14 388:24
353:2,17,20	406:12 451:13	105:22 117:5	208:14	408:22 417:6,6
354:7 359:10	468:16,18	120:9 141:23	memorize 41:7	417:9,10 425:5
359:12,13,23	469:6	151:23 152:5	341:8 441:12	425:16 454:23
360:14 361:2	measure 333:2	152:10,18,22	memorized	455:3
363:7 367:19	340:22 363:22	153:15 154:7	36:25 37:5	Metals 10:24
370:21 372:4	403:5,17	154:16 155:10	memory 37:9	393:16
372:19 373:24	405:15 406:2,6	155:16,18	68:25 380:10	meter 376:1
376:3 379:2	406:10 460:25	156:4 157:3,8	424:21	404:20
380:7 382:5,20	461:13,14	158:9 159:7,20	mention 292:12	method 244:23
383:23 386:23	measured 406:9	161:12 162:5	458:6	363:4 421:5
387:2,2 392:11	measurement	162:19 163:21	mentioned	methodologic
392:13 401:13	404:1	164:10 165:5	46:14 154:22	191:9
401:14 402:25	measurements	165:21 166:25	162:13 259:2	methodology
407:1 409:19	391:12	167:21,22	280:16 331:13	143:19,25
409:23 412:8	measures	168:3,17	339:22 363:17	238:9 243:3,6
415:13,19	239:15,23	170:23 176:14	397:23 469:4	243:12,20,22
419:4 421:15	392:23	177:8 178:22	Merlo 228:23	243:24 244:13
425:6 433:15	mechanical	179:7,14	Merritt 351:12	methods 143:18
435:11,21,21	468:1	188:20 189:6,8	meso- 137:2	143:22,22
435:22 437:7,8	mechanism	190:15,19,20	meso/asbestos	144:7,13
443:23,25,25	165:3 281:17	194:9 215:3	207:14	253:25 266:13
445:14,19	384:7,20	222:4,21,23	mesothelioma	291:10 292:21
448:13 449:11	385:23 414:16	223:16,17	11:7 55:15	404:10 448:8
452:23 454:13	415:23 417:14	228:12 229:21	124:6,10,13	metrics 405:5
455:9,10 459:2	418:2,17	408:12 412:16	125:19,21	MHS 6:13,17,20
459:6,8 463:3	433:20 443:11	436:9 468:8	128:25 137:3	7:10,17,21

9:16 95:2 206:15 mic 14:9 Michelle 3:4 53:6 microgram 404:20 micrograms 375:25 Microphone 14:7 89:10 377:22 microscopy 11:17 427:11 middle 151:12 284:1 294:4 midpoint 351:7 migrate 281:3,7 411:11,23 412:17 415:18 416:7 428:8 429:7,16,19 432:3,10 433:7 434:1 435:1,24 436:13,25 449:16,25 452:18 453:20 migrated 412:24 migrating 435:17 migration 254:5 418:16 422:12 425:20 439:7 441:16,25 448:7 452:15 MILLER 5:9 27:6 53:6,9,12 53:16,20 67:17 86:5 111:6 112:17 116:15 116:18 132:14 132:19 204:5 348:20 440:13 465:20 million 263:1 Mills 351:12 mind 86:13	385:22 mine 21:22 85:7 85:9,12 95:6 153:2 188:17 208:12 215:25 335:19 348:20 388:5 mineral 74:2 75:25 76:13 120:4 mineralogist 73:10 119:15 120:4 minerals 73:25 120:15 125:24 minimal 456:23 457:4,21 minimum 391:2 minus 420:22 minute 25:24 200:13 247:7 251:1 286:15 293:2 299:22 299:25 318:2 361:25 369:15 minutes 299:19 377:1 misclassificati... 387:15 461:9 misclassify 461:12 misdiagnosed 395:12 misdiagnosis 395:22 396:6 misheard 307:16 misinform 306:2 mislead 274:2 misquote 280:17 misreading 332:8 misrepresent 329:20 misrepresenta... 310:19	misrepresenting 161:22 330:5 misrepresents 295:24 missed 100:5 182:16,22 366:10 missing 199:8 misspoke 126:22 345:12 misstate 453:8 misstates 20:23 67:16 88:7 129:19 132:12 150:22 151:7 153:17 172:12 176:3 224:2 225:3 256:17 264:4 265:2 272:17 274:1 275:5 276:4 279:8 298:21 299:3 315:5 323:21 336:22 429:14 432:5 434:3 436:17 437:4 449:7 misstating 279:14 mistake 287:5 292:11 293:18 mistaken 67:6 misuse 295:16 295:20 298:13 310:17 MITCHELL 3:13 mixed 421:19 450:1 mixture 454:12 mm-hmm 25:3 69:24 77:20,22 144:3 255:25 256:6 259:11 283:25 295:2 309:1 311:10 314:1 320:5	331:12 347:19 349:17 365:11 386:20 397:24 402:22 442:12 448:18 model 24:21 178:19 450:3 modern 8:19 290:2,18 388:2 418:8 modifiable 263:19 264:2,3 modification 347:4 modified 334:9 modify 340:8 mold 203:17 molecular 253:20 255:13 255:16 moment 24:25 29:10 34:2 44:11 151:23 209:25 216:6 238:8 241:7 244:17 256:4 298:10 355:15 355:16 365:7 402:23 438:23 440:1 447:9 464:18 money 179:23 179:24 monitors 404:19 monogram 259:6 monograms 259:6 monograph 10:23 259:8,9 259:9,10,19 401:1 monographs 239:3 259:23 month 231:12 months 264:21 Moorman	346:14,17,18 349:14 351:13 morbidity 40:21 40:23 morning 14:2,3 17:13 19:15 439:3 morphed 275:8 mortality 10:9 40:21 41:2 366:3 367:3 389:5,8,18 395:1 mother 403:24 MOTLEY 4:10 mouse 102:16 107:22,25 253:9,9 mouth 58:12 mouthful 310:3 move 19:3 39:7 46:17 101:17 151:15 161:7 176:7 190:14 280:8 310:6 383:17 398:5 398:13,17 movement 312:7 314:18 moving 8:23 9:10 280:3 296:25 308:18 309:2,2,22 MSA 40:4 166:14 173:1,2 173:4,16 174:21 175:3 175:18 176:1 176:12,20 177:6,14 178:3 178:4,9 180:12 180:18 181:7 181:12,13 182:1 185:14 185:18 186:3,9 186:23 187:1,5 187:18,19
---	---	---	---	---

191:15,16,18	109:15 135:18	85:20 92:4	Nicole 309:8	27:25 28:7
192:1,7,16	271:25 273:13	275:17 300:13	nicotine 404:23	29:5,11 31:12
193:10,11,25	296:9 297:10	300:15 326:13	405:18 406:7	287:9 334:24
194:6,8,15,20	297:22 305:10	335:5 438:19	406:10,10	465:22 471:11
194:23 195:1,4	317:3,16,20	neighborhood	NIH 10:13 320:4	notice 2:16 6:11
195:13 197:21	nearby 48:18	387:17	NIH's 320:7	6:15 16:13,18
199:6 200:5,14	nearly 344:15	neither 120:5	NO2 102:14	16:23 17:15
468:8,14 469:6	necessarily	305:23 362:23	node 412:25	27:23 29:1
469:13 470:5	27:25 51:23	neoplastic 34:25	nodes 11:19	notion 411:4
MSA's 195:23	76:17,25	35:6	123:3 412:17	novel 320:1
multidistrict	179:13 204:4	Ness 351:11	427:12 428:9	November 67:1
129:17	216:12,13	442:20 444:17	429:8,20 430:4	67:13 68:9
multiple 171:11	224:16 352:11	Ness's 443:17,21	noise 301:7	69:12 70:20,20
408:5	412:8	444:2,2,5,16	non-exposed	71:1,8,19
mutagenic	necessary	never 10:6 57:21	284:10	NSAIDS 172:23
418:10 444:20	319:13 362:23	184:20 189:10	non-pulmonary	421:17,22
muted 460:2	363:3 391:3	189:11,12	199:2,15,17	NTP 262:2,13
mutual 33:2	456:25 472:3	192:1,6 236:18	200:6,20,23	439:12
	need 24:8 25:1	266:6,12	non-serous	nuanced 217:1
N	53:20 68:5	299:21 300:12	414:18	256:20
N 3:1 6:1,1 13:1	72:20 79:5	304:13 305:19	nongenital	null 352:8,18
N.W 3:7 5:11,18	82:13,18 83:18	364:11 365:5	414:17	382:15,21
name 13:4 15:25	85:25 86:23	365:13,14,16	nonsense 277:1	number 8:13
92:17 93:24	88:22 99:18	366:20,22	nonsmokers	20:3 26:13
107:10 138:11	118:21 133:4	428:3 430:9	379:12	32:14,19 33:1
152:25 174:20	157:23 190:16	438:17 440:17	nonstatistical	35:13 37:6
187:23 188:21	191:9 193:2,25	442:5	357:19	40:23 41:6
285:10 288:24	268:18 299:22	new 1:2 3:22	nonstatistically	97:3 122:15,16
289:9 294:4	300:6 304:4	4:21 5:11	321:7 322:7	122:18 123:1
295:11 312:23	323:12 329:13	13:15 36:20	Nope 346:17	123:15,16
313:8 326:23	338:9 341:13	93:15 182:1,4	354:9	138:16 172:15
366:17 465:1	347:13 372:2,7	303:6 316:23	normal 182:9	179:4 183:12
471:14	386:4,5,6	364:16,16	215:9 226:13	247:22 248:1
named 175:9	397:10 401:23	401:14	normally 15:5	248:11 249:22
names 196:17	405:6 430:15	newly 376:11	North 2:5 13:9	282:13 331:16
253:6	431:19 438:16	Newport 4:6	Nos 377:16	340:13,18
napkin 332:24	440:3 446:1,3	Newton 285:8	nose 58:12	351:7 361:11
334:23	446:10,12,13	nice 93:13	Notary 2:17	375:25 404:12
napkins 331:14	450:18,18	181:23 204:13	474:19	413:25 414:2
332:21 334:17	451:8 461:14	Nich- 83:8	notation 216:2	420:25
narrative 32:19	467:4	Nicholson 7:7	notations 31:10	numbers 37:1
narrow 237:7	needed 191:18	81:7,8,9,16,22	note 29:17 153:4	257:16 345:9
Nate 465:2	194:8 255:9	86:9 87:16	noted 13:18 68:2	346:12,13
NATHAN 4:9	452:13	88:4	128:2 394:22	379:23 380:6
National 262:3,5	needless 78:19	Nicholson's	472:9 474:7	389:7
262:9	79:5 84:23	82:12 83:15	notes 26:3,6,11	numeral 276:15
nature 103:25	needs 83:5,17	84:4	26:14 27:18,24	numerous

451:22	72:8,19 73:6,7	186:10,12	267:18,19	380:23,24
NW 4:11	74:13,17,24	187:20 188:5	268:2,12 271:6	381:3,8,20
O	75:8 78:20	188:11,23	271:7 272:16	382:2,3,16
O 6:1 13:1	79:2,21 82:1	189:2 190:22	273:23,25	383:6 384:9,22
oath 2:18 13:21	88:5,6 89:25	191:20,21	274:4,16,17	384:25 385:15
160:5,24	90:1,15 96:17	192:3,4,10,17	275:4 276:3	385:25 389:9
object 32:17	97:22 98:7	192:20 193:20	278:11 279:8	390:20 391:4
33:7 35:16	104:2 105:10	194:1,11 195:5	281:8,15	391:25 396:8
37:14 80:16,24	106:6,22 107:4	195:14,18	282:21 286:10	396:15 399:23
83:14 112:23	107:16 109:4,9	196:2,10	287:6,25 288:9	401:10 402:9
112:23,25	109:18 110:1	197:13,17	289:2,8,13	402:10,18
113:6 129:15	110:12,15,18	198:7,21 199:3	291:12,13	403:8 405:12
131:17 158:11	110:24 111:5	199:16 200:9	292:4 293:1	406:20,21
260:5 279:13	111:11,19,23	201:12 202:1,5	295:22,23	407:9,10 408:3
310:5,18 326:8	114:4,9 115:25	202:9 203:3	298:19,20	408:4,23
326:17 378:20	117:11,20	205:10 206:19	299:2,12	409:13 410:5,8
425:23 427:25	118:1,12,25	207:18 208:20	301:18 302:18	410:25 411:1
429:2 438:11	119:9 120:17	209:3,9,20	304:3,24,25	411:13,14,18
441:18 448:11	123:25 124:23	210:11 215:16	306:6,7 307:1	411:25 412:1
464:9	125:8,14	216:10 217:12	307:2,7 314:10	412:19,21
objected 154:3	126:21 127:13	218:5,6 219:11	314:25 315:5	413:13,14
objecting 32:5	127:21 128:21	220:16,17	318:13 319:19	414:25 416:1
33:21 35:19	129:9,18 130:2	221:19 222:8	321:10,21	416:13 417:24
83:21 160:10	131:11 132:12	222:25 223:7	322:9,21	417:25 418:19
326:11	134:21 137:22	223:24,25	323:21 325:8	418:20 419:6
objection 15:18	140:23 141:13	225:2,17 226:2	326:7 329:12	420:12 421:6
16:3 18:4	143:3,6 144:20	228:8,13	330:22 331:4	422:14,16,25
20:22 21:17	145:8,16	229:22 230:19	333:19 334:10	423:4,11,24
22:7 23:19	146:13 147:8	231:3,18,19	334:20 336:21	424:15,17
35:7,25 36:24	147:18,23	232:16,17	339:4,17,25	428:18 429:14
38:1,4 39:9,19	148:18,25	233:1,12 234:1	340:6,11	430:6,7,12
40:16 41:15	149:15,23	234:2 235:5,6	342:18 343:18	432:4,5,13,14
42:19 43:20	150:21 151:6	236:25 244:2	345:7,22 346:8	433:13 434:3
47:6,22 49:5	153:17 155:1	245:25 246:10	347:12 352:3	434:15,21
49:21 50:4,21	157:10 158:14	247:24 248:7	352:10 353:11	435:5,7,19
50:24 51:9,19	159:13,23	248:17,23,24	354:4 356:25	436:15,16
54:3,14,25	160:12 166:3	249:6,11,17,24	357:13 360:13	437:3 442:1
55:8,16 56:2,8	168:19 169:13	250:6,21 251:5	361:24 362:10	443:18,22
56:19 57:14,23	169:20 170:15	254:17 255:2	362:25 363:13	444:7 445:3,4
58:14 59:5,12	171:16 172:11	255:15,22	364:2 367:8,18	445:16,17
60:4,17 61:4	174:6 175:5,12	256:17 258:4	368:7,19	446:4,5,21,22
62:4 63:24	176:2,15	260:10,25	371:19 372:1,4	447:18 449:5,6
64:6 65:1,12	178:12,24	261:1,16,24	372:14 373:3	450:9,10,22,23
65:19 66:21	179:8,17	262:19,24	373:17,22	451:10 452:1,2
67:15 68:11	180:25 181:9	263:20,24	374:9 375:8,10	452:20 453:6,7
69:14,20 70:22	182:18 183:1,7	264:4 265:1,2	375:14,20	453:21,22
	184:4,18	265:20 266:1	376:16 380:4	455:7,16,23

456:18 457:8	offering 301:5	29:2,18 30:14	132:2,23 133:6	207:9,13,16,25
457:23,24	offers 309:6	30:22 31:8	133:23,25	208:7,23
458:21 461:10	439:6	32:18 33:11,24	134:18,24	209:16,23
463:20 464:5,6	office 30:11	34:8,12,17,23	135:13 136:5	210:3 212:1,4
466:4,25	154:20,22	35:22 38:16	136:22 137:5	212:15,23
467:11,12	officer 81:12,16	40:10,20 43:12	137:19,25	213:3 214:2,15
470:1,8	official 439:4	43:18 44:1,24	138:3,6,11,14	216:7 217:7,18
objectionable	officiated 2:18	45:16 46:20,25	139:8,9 140:2	218:23 219:18
37:21	Ogburn 312:22	47:17 48:4,5	140:7,10,16	220:4,7 221:12
objector	oh 26:20 43:5	49:25 50:11	143:18 144:11	221:17 222:1
115:12	44:23 53:11	51:14 52:2,19	145:5,25 146:6	225:19 226:11
objections 18:5	58:19 62:13	53:22 54:1,16	146:23 147:1	226:24 227:3,8
32:1,19 75:17	66:13,17 67:23	54:16,22 55:5	147:16 148:9	227:11,12,20
161:4 326:16	69:21 76:22	55:24 56:5,12	149:20 151:9	228:11,16
471:7	81:14 86:15	57:20 58:5,7	151:25 152:5	229:2,10,13,16
objective 35:11	91:1 94:9	58:24 59:9,20	152:16 153:14	229:19 230:6
35:14 41:3	98:19 99:20	60:11,25 61:8	154:3,11,21	230:15 231:9
observed 395:13	112:8 113:17	63:1 64:3 65:8	155:4,9,14	231:10,25
445:22 446:15	128:8 136:3	66:2,7 72:14	156:3 157:8	232:10,21
obstetrics	139:7,8 165:11	73:17 75:3,15	158:7 159:16	233:7,19
105:23 239:4	167:14 170:5	75:23 76:11	162:19 164:21	235:16 236:4
obstructing	174:7 175:4	77:6,21 81:15	165:14,23	236:12 237:10
133:4	182:11,13,17	81:21 82:6,20	168:8,11 169:2	238:7,9,16
obstructive 96:9	186:15 188:10	83:10,24 84:1	170:23 171:6	239:25 241:1
97:17 100:23	209:8 212:15	85:13 87:9,15	171:11 173:13	241:21,25
101:10 103:5	220:25 240:25	88:15,16,20	174:14,24	242:9,23 243:5
obtaining 154:4	242:8 264:15	91:2,10 92:5	175:2,17	244:5,24
obviously 22:13	270:8 276:10	93:2,18 95:1,4	177:16 179:4	247:15,19
97:24 185:15	284:24 297:4	95:8 96:23	179:12,19	248:10 249:8
206:7 241:14	307:20 325:19	97:5 98:3,20	180:15,22	249:14 250:3
244:22 336:25	341:8 342:8	98:22 100:4,12	181:12,15,25	250:25 252:5
338:21 433:21	343:17 348:15	101:2,7 102:6	182:21 183:5	252:24 254:3
434:6 451:15	350:23,24	103:1,14 105:7	185:12,17,24	254:12 255:18
occupational	351:3 352:24	105:16 106:18	186:8,17,21	256:8 257:2,6
395:1	354:21 366:8	107:2 108:2,18	187:1,17 188:1	259:2,22
occupationally	374:12 375:15	109:1,24 110:5	188:19 189:6	260:21 261:7
284:4	383:4 389:18	111:21 113:1	189:11,15	261:12,21
odd 435:9	398:7 406:25	115:22 116:12	190:7,13	262:5 263:15
odds 333:11	410:9 414:4	117:9,15 118:8	191:13 193:14	264:9,13,20
347:8,16 349:9	416:12 424:3	118:19 119:5	193:24 194:4	265:6,12,17
349:15,24	429:22 433:2	119:15,21,25	194:19 195:12	267:5,14
351:12 361:4	437:13 441:3	120:3,8 121:8	196:25 197:5	268:10,17
365:12 368:21	okay 16:11	121:19 122:12	198:17,25	269:14 270:7,8
offer 179:20	17:11 20:10	125:5 126:5,7	199:10 201:15	271:9,12 272:9
342:5	23:15 24:24	128:2,9,13	201:21 202:14	273:18 277:18
offered 158:3	25:23,25 27:11	129:11,24	203:14,20	278:25 279:24
184:11	27:15 28:3,10	130:24 131:8	204:17 205:13	280:2 281:2,13

282:8,11 285:3	367:25 368:14	184:8	400:13 401:8	240:1 243:14
287:2,11,21,24	368:24 369:2	onc 63:14	421:3	317:1 320:9
288:22,25	369:21 370:11	oncological 62:2	opinions 22:5	321:2 343:12
289:6,11,17,19	372:10,22	oncologist	70:16 71:3	372:8 383:11
290:5,9,21	376:21 378:11	115:16,17,18	76:2 88:13	386:18 391:3
293:22,24	378:18 381:23	oncologists	166:15 170:3,5	405:10 406:1
294:1,6,10,24	382:19 384:2	60:20,22,25	183:20,20	406:17 407:6
295:2,2,9,14	385:7,10,20	oncology 63:7	199:2,14 205:4	407:24 446:1
296:3,6,22	386:21 388:14	104:23	205:13,19,21	446:14 450:7
297:6,12,24	389:2 390:9,25	one-page 440:5	206:8 207:11	450:19 451:8
298:2,5,9	391:16 392:16	ones 30:8 61:6	207:14 208:8,9	461:13 467:5
299:10,18	392:24 393:19	69:4 109:5	208:13,17,24	ordinary 205:8
300:20 301:14	394:5 395:5,17	123:11 147:13	208:25 209:18	organ 104:13,14
301:25 303:18	395:19 396:1	240:23 245:2	210:4 211:7,13	organization
303:23 305:5,9	396:12,18,22	247:10 252:7	215:13,13	260:4,9,19
305:12,15,18	396:23,24	252:18,19,19	222:24 227:25	organizations
306:22 307:5	397:4,13 398:5	253:5 259:24	228:2,7,12,18	260:12
307:10,13,25	398:9 399:10	259:25 348:17	232:6 233:10	organize 153:24
309:19 312:4	399:20 400:18	355:9 357:3,5	238:10,11	157:22
312:18,22	400:24 401:16	371:5 376:12	243:16 251:17	organs 428:8
313:3,11 314:8	402:4,14	389:23 390:5	255:4,20	429:7,20
314:8,16 316:6	403:17 406:5	392:22 412:3	256:15 261:22	original 147:17
318:8,18	407:4 408:18	449:11 452:5	286:18 360:4	147:22 148:5
320:14 321:16	408:21 409:2,8	ongoing 128:20	384:19 390:18	149:12,14,17
322:16 324:2,9	410:17 411:21	128:24 129:3	407:7 436:20	257:15 401:11
324:10,11,15	413:4,7,20	Oops 368:8	438:18 462:16	471:12 472:11
327:17 328:8	414:10,22,24	open 181:19	469:18,23	Originally
328:13,15,25	416:3,16 417:5	217:2	470:3	296:11
329:4 330:16	417:23 419:22	opened 69:5	opportunistic	ought 353:21
330:19 332:1	419:24 420:18	operation	410:1	outcome 270:11
333:16 334:15	422:20 425:13	191:11	opportunistic	270:17 371:13
339:1,8,20	427:23 428:22	opined 76:12	409:22	448:1 459:9,20
340:4 342:16	429:6 431:3,12	436:9 453:3	opportunity	outcomes 103:6
343:14 344:3,8	431:21,25	opinion 35:4,10	114:6 193:9	270:9
345:3,20 346:2	432:20 433:4,5	56:17 57:11,21	298:2,6 409:4	outdoor 376:10
346:25 350:3	433:12 437:12	59:1,9 60:1	409:8 427:20	outpatient
350:11 351:18	438:14 440:18	68:15 70:12	opposed 185:1	105:13
351:24,25	441:7,10	71:15,24 72:2	242:21 263:7	outside 134:19
353:7 355:10	442:15 443:2,8	78:2,9 211:25	339:23 401:22	154:20,22
355:11,13,14	443:14 444:15	212:16,25	opposite 359:9	208:25 409:17
355:19 356:20	445:2,25 448:4	219:7 221:5	462:25	ovarian 6:24
357:17 360:2	451:21 454:9	243:1 252:2	Oral 6:11,16	8:17 9:20 11:5
360:11,18,24	456:21 457:4	255:7 256:18	17:15	11:9,13 12:5
363:23 364:7	457:20 458:8	271:3,4 281:2	order 47:1,19	28:14,18 34:24
364:18,25,25	459:23 460:1,8	281:6 306:16	80:5 90:7	35:5 36:6,9,13
365:2,15,22	464:1 467:7	318:8 356:20	176:1 180:12	36:20,23 39:16
366:1 367:6,13	omitted 183:13	370:17 399:21	191:18 238:10	40:13,21 41:11

41:14,21 45:8	247:23 248:5	435:18,25	p.m 89:4 204:20	172:5 324:4
45:20 46:1,22	250:4 263:16	436:14 437:1	204:23 280:11	325:4 336:18
51:18 55:7,15	271:20 272:15	437:10 449:17	280:14 320:18	414:11 474:3
59:10,18 60:3	273:22 274:15	449:20 452:18	320:22 338:13	paid 23:24
60:15 61:2	275:2 276:2	453:20	338:17 377:9	197:21 430:17
62:3 63:12,18	278:4,22 279:3	ovary 282:12	377:12 426:16	pair 388:1
75:6 76:3,14	281:24 282:14	283:9 394:24	426:19 447:10	PAPANTONIO
79:11,15 89:24	285:14,18,21	448:9,16 449:2	447:13 464:12	3:13
109:21 111:3	358:3 359:3	overall 383:3	464:15,19,22	paper 29:21,22
111:10 115:24	368:17 384:8	463:11	470:17,21	30:2 124:12,12
116:7 117:1,4	384:21 385:24	overbreak	page 6:2,10 7:3	144:18 145:10
117:19 118:10	386:11,18	203:25	8:3 9:3 10:3	147:14 182:3
118:21 119:3,7	387:6 388:7,25	overhead 45:17	11:3 12:3 19:4	182:12,13
124:18,22	391:3,11,17,23	85:18,23	21:15 42:9,15	257:15,23
125:2,7,12	392:8 394:2	overlap 245:14	42:20,24 43:10	264:9,14
126:10,15	395:12,23	overlapping	45:13 65:22	276:25 277:1
127:12,20	397:17 398:1,2	404:10	76:7 83:9,14	298:15 315:13
129:7,13 130:1	398:10,14,23	overly 64:6	85:1 87:11	316:21 320:10
131:1,14 132:8	399:10,15,17	287:17 306:8	98:1 99:21,24	321:2 330:5
134:10,16,19	399:18 400:19	Oversight	100:7 140:5,9	332:5 342:15
135:5,15 136:8	401:9 402:8	231:13	171:4 181:19	370:15 371:3
136:17,20,21	406:13 407:8	Overview 102:3	206:17,22	373:10 375:3
137:21 138:8	410:18 411:4	102:10	208:2 209:23	393:5 423:12
140:22 142:12	413:12 415:9	Ovulation 6:23	210:25 211:21	425:1 439:3
147:22 148:17	415:24 417:12	45:8	212:2,3 214:16	444:2,2,5
149:22 150:13	417:15,20	oxidative 102:19	243:6,6,8	papers 20:15
150:20 151:4	420:4 421:8,10	444:18	244:7,10,10,14	92:1 121:20
163:7,13,19	422:24 423:10		246:6 247:16	124:5,21
164:12 165:25	423:15,18	P	247:22 248:4	125:12 143:22
167:3,12	428:7 433:6	p 3:1,1 8:23 9:10	256:5 269:8	143:24 144:6
172:24 187:7	439:9,13	13:1 296:25	271:10,13,14	144:24 145:12
198:25 199:11	442:20 443:12	302:14 308:18	277:14,15	145:14,19,20
200:1,4,6	444:23 451:24	309:3,23	290:22 325:11	145:21 146:7
201:5,9,24	453:5 457:6	311:15 318:25	325:13,13	146:10 147:5
202:22,22	460:11 462:19	319:13	326:1 328:24	163:25 164:1
203:2 209:18	464:4	p-value 295:21	343:21 369:22	164:17 182:11
210:23 211:20	ovaries 273:1	298:14 302:13	393:20 394:6	240:12 298:17
212:22 214:11	280:21,25	305:21 312:8	396:19 397:15	301:10,16
214:12,24	281:3,7,14	316:12,16	399:5,7 400:21	317:3 321:4
215:8 216:21	283:20 284:8	318:19 319:3,9	416:24,25	337:4
217:10 218:3	284:14 411:12	361:8	433:2,3,3	paragraph 76:9
219:9 220:12	411:24 412:17	p-values 295:17	440:11 441:4	101:7 176:9
221:7 226:12	412:25 415:5	301:5 302:5	443:2 444:15	181:22 212:6
233:23 234:15	415:18 416:7	303:5 309:12	473:4	212:14 236:8
234:21 236:17	418:18 422:13	309:25 315:11	pages 26:3 85:4	244:21 271:14
237:19 240:16	423:18 430:4	316:1 317:1	86:9 99:22	277:21 282:10
240:25 241:5,9	432:3,11	P.A 3:14	170:11,11	283:24 284:2

Gregory B. Diette, M.D.

Page 512

292:10 300:24	48:19 49:16,24	113:1,4,10,13	167:11 169:1,6	227:13 228:10
329:21 400:21	50:5,22 51:3	113:16,20,24	169:9,16,24	228:15,22
400:23 414:21	51:13 52:1,4,6	114:3,14,18,21	170:22 171:18	230:5,24 231:8
419:16 420:15	52:13 53:2,8	114:22,24	172:16 173:24	231:24 232:4,9
432:23 469:9	53:11,15,19,22	115:3,5,15	174:13 175:7	232:20 233:2,6
paragraphs	54:8,9,15 55:4	116:2,19	175:16 176:11	233:14,18
243:7,9	55:10,23 56:4	117:14,23	176:20 177:1	234:7,19,24
paraphrase	56:11,25 57:19	118:4,18 119:4	177:12 178:21	235:1,2,15,20
408:10	58:2,9,17 59:8	119:10 120:19	179:3,11,18	237:9 244:4
paraphrasing	59:19 60:10,24	124:3 125:4,10	180:9 181:3,11	246:3,24 248:3
293:6 452:11	61:7,15,20,22	125:16 126:23	182:20 183:4,9	248:9,19 249:1
pardon 76:19	62:8,13,19,25	126:24 127:1,2	184:5 185:4	249:7,13,20
325:16 437:22	64:2,11 65:6	127:16,24	186:13 187:16	250:2,9,24
parens 102:14	65:15,23,24	128:23 129:10	187:25 188:18	251:8,25
102:15,15,16	66:20,22 67:23	129:16,23	188:24 189:5	254:19 255:12
397:18	67:25 68:2,3	130:4,9,13,17	190:6,9 191:12	255:17,25
parent 404:11	68:16,18 69:18	130:23 131:7	191:25 192:8	256:2,3 257:1
parentheses	69:23 71:2	131:13 132:1	192:14,18,23	258:5,16 259:1
211:18,19	72:13,24 74:9	132:16,23	193:4,7,23	259:9,11,14
parents 16:7	74:14,20 75:2	133:5,14,22	194:3,18	260:7,16 261:6
403:23	75:14,20 76:19	134:23 135:4	195:11,15,24	261:20 262:1
Parfitt 3:4 6:3	76:22,24 78:23	136:1,14	196:4,8,24	262:22 263:3
14:1,8 15:22	78:25 79:12	137:15,24	197:15 198:4	263:22,25
16:5,10,16	80:7,20 81:1	138:20,25	198:16,24	264:8 265:5,24
17:21 18:7,10	82:6,16,20,24	139:3,8,10	199:5,17,21,22	267:4,11,22
19:1,9,20,25	83:6,7,19,24	140:7,10,12,15	200:11 201:14	268:5,16 269:2
20:2 21:10	83:25 85:13,17	141:5,16,19,21	201:20 202:3,6	270:4,6 271:8
22:1,15 23:25	85:22 86:4,7	143:4,17,23	202:13 203:6	272:4,5 273:17
24:13,16,23	86:19,22,25	144:3,10 145:1	203:11 204:11	273:25 274:4,7
26:18 27:8,14	87:4,9,10	145:11,24	204:15,18,24	274:21 275:10
27:17 28:25	88:14,21,24	146:22 147:2,3	205:12 206:6	275:14,18,21
29:8 31:2,9	89:2,8,11	147:15,20	206:12,23	276:5,14
32:4,12,18,23	90:12,23 91:7	148:3,20 149:7	207:24 208:22	277:13,21,24
33:11,17,24,25	95:10,12,16	149:19 150:1	209:6,15,22	278:8,24
35:15,18,20	96:22 98:2,10	150:16 151:1,9	210:15,18	279:23 280:5,8
36:4 37:7,15	98:12,14,16	151:11,14,21	211:1,4,6	280:15 281:12
37:19 38:1,10	99:3,7,13,17	152:15 154:2	213:6,11	281:21 282:2
38:13,16,20,22	100:10,13	154:11,15	215:21 216:17	283:2,5 286:14
38:25 39:3,8	102:7,9 103:23	155:3 156:12	217:13,23	287:9,20 288:6
39:12,13,23	103:24 105:6	156:14,18,21	218:1,10,13,16	288:14 289:5
40:19 42:1,11	105:15 106:17	157:2,14	218:21 219:2	289:10,16,24
42:13,23 43:3	107:1,12,19	158:12,16	219:13,15	290:25 291:2
43:8,13,25	108:9,25 109:6	159:6,15 160:3	220:3,20	291:18 292:3,6
44:11,22,24,25	109:12,13,23	160:12,14,18	221:25 222:19	293:7 295:25
45:6,14,15	110:4,13,19,25	160:21 161:2,6	223:5,12	296:21 297:16
46:17,19 47:8	111:8,13,20	162:1 166:3,7	224:19 225:11	297:20 298:23
47:12,16 48:1	112:3,6,15,19	166:10,18	225:18 226:10	298:25 299:9

299:15,24	362:20 363:9	426:22 427:7	239:20 240:19	369:6 372:18
300:3,8,14,16	363:16 364:6	428:2,4,21	241:19 242:3	373:24 375:25
300:19 301:24	366:13 367:9	429:5,11,18,24	243:2 244:6	376:1 406:1
302:23 303:17	367:24 368:13	430:2,13,18,25	248:6 252:24	421:20 423:19
304:6,10,15,19	368:23 369:18	431:9,12,16	252:25 255:23	434:9
305:4 307:4,9	371:22 372:3,9	432:7,19	260:18 265:11	particularly
308:4,9 310:6	372:21 373:5	433:24 434:10	268:3 273:11	108:4 285:25
310:9,10 311:9	373:19 374:3	434:16,23	273:12 283:3,3	414:18
312:11,16,19	374:10 375:12	435:13 436:3	283:6 293:4	particulate
314:15 315:2	375:16 376:13	436:23 437:11	295:1 303:9	10:15 102:14
315:23 318:17	376:20 377:4,7	437:15,22,25	310:25 311:7,7	103:7 120:11
319:21 320:15	377:18,23	438:13,21	313:24 315:12	284:19 285:6
320:23 321:15	378:16,22,23	439:20,22	320:16 321:13	285:12 368:25
322:3,15,24	380:9,17 381:1	440:5,8,11,18	321:14 322:12	370:5,18 371:8
324:1,20,25	381:5,12,22	440:22,25	337:1 387:5	371:24 372:12
325:3,9,16,19	382:10,18	441:19 442:11	399:15 408:9	372:23 373:21
325:23 326:5,8	384:1,13,24	442:24 443:3,5	417:8 467:2	374:8,17,24
326:15,19,21	385:11,19	443:20 444:4	part- 435:17	375:19 376:6
326:24 327:1,2	386:3 389:13	444:11,14	participants	376:10 404:19
328:1,3,13,16	390:3,8,24	445:13,24	249:15 270:10	404:21
329:16,19,22	391:15,21	446:7 447:8,15	participate	particulates
330:2,6,9,23	392:5 393:12	448:3,17 450:5	63:14	370:25 435:1
330:25 331:1,7	394:16 396:11	450:14,17	particle 371:15	parts 217:17
331:20,24	396:17 397:3,6	451:6,20 452:7	388:11,11	219:1 379:1,4
332:2,5,9	397:9,12 399:5	453:1,11,24	particles 215:7	partway 454:22
334:6,14 335:3	399:6 400:1,17	455:12,18	225:23 254:8	party 64:10
335:7,10,13,14	401:12,14	456:4,20 457:3	373:15,15	pass 52:20
335:18 336:6	402:3,13,21	457:19 458:2	412:9,10,16	passed 302:13
337:9,12,17,21	403:11,12	459:1,5,22	428:24 429:7	passing 86:13
337:25 338:4,6	405:9 406:4,23	461:7 462:14	433:7 435:17	passionate
338:11,18,19	407:12 408:7	463:25 464:8	448:21 449:24	306:15
339:7,19 340:1	409:1,25 410:6	464:11 470:1,8	particular 46:9	passive 365:4,16
340:7 341:4	410:16,21	470:12,15	68:21 69:3	passively 284:5
343:13 344:2	411:6,16,20	part 24:20 31:12	70:4 74:1,2	pathologist
345:8,14,24	412:13 413:1	31:13 43:6	92:14 105:24	119:11
346:10,15,19	413:19 414:2,6	46:18 48:10	107:21 133:3	Pathology 11:15
346:23 347:1,2	415:6 416:2,15	60:7 63:6,15	163:10 172:21	427:9
347:18 348:11	416:21 418:12	65:17 70:12	176:9 181:6	pathophysiolo...
348:22 349:1,2	418:24 419:9	79:5 91:25	190:17 194:7	444:22
349:12,16	419:17,19	92:21 93:5	223:13 230:13	pathway 447:25
350:17,20,23	420:16,19	117:6 123:13	233:11 238:6	449:4
350:25 351:5,8	421:1,9 422:6	138:16,17	240:7 270:17	patient 104:24
352:6 353:6,13	422:18 423:2,5	149:11 195:19	277:11 311:19	335:21 405:6
354:5,19 356:6	423:21 424:1	197:22,25	312:2 333:5,6	patients 103:17
357:6,16	424:18,22,24	202:23 221:23	342:4 343:9	104:1 105:21
358:10,16	425:25 426:4,5	222:3 225:19	358:4 359:1	Patricia 328:5
360:17 362:2	426:9,12,15,21	226:8 230:9,13	361:6,17 369:2	patterns 102:21

108:3	143:9,11 157:1	perineum	162:14 173:15	251:17 343:8
Pause 19:12	168:14 169:22	284:20 285:7	phonetic 313:1	410:12 431:18
44:17	170:13 190:21	285:17 411:15	454:24	460:1 461:24
pay 14:19	191:3 196:14	411:17 412:23	photocopying	planning 318:15
158:22	226:7 239:9	433:8 435:2,24	178:17	plans 257:6
paying 139:19	261:5 263:2	437:9 449:19	physical 469:12	320:2
pays 192:9,15	268:22 287:15	period 21:1	physician 34:15	plastic 186:20
PC 3:20	288:19 303:8	41:13 45:19,25	118:22	plausibility
PCPC 5:15	311:1,13 312:2	117:16 420:2	pick 319:9	272:25 273:4
110:14	314:2 316:8	periods 257:24	333:14	418:25 419:4
pedantic 301:3	319:2 332:23	258:9	picked 342:3	433:20 445:14
peer 319:10	333:5 340:19	peritoneal	picking 106:8	446:16,19
408:19	341:3 343:3,23	395:11,22	304:18 343:1	447:17 449:1
peer- 121:20	344:14,15	411:11 433:8	picture 54:11	451:5
257:22	361:9 372:17	435:2 457:25	pictures 51:10	plausible 89:22
peer-reviewed	386:15 404:15	peritoneum	piece 306:16	384:7,20
121:11,16	406:9 409:17	126:2	341:9 357:1,2	385:22 386:14
123:21 124:5	415:19 436:20	person 51:24	357:15,15	414:16 415:23
124:17,21	437:7 442:7	57:7 63:4 80:4	359:19	416:6 418:17
125:6,11,18	447:2 459:14	91:12,14	pieces 244:25	420:10 421:4
126:8,13,18	466:6	106:15 113:6	339:9 470:6	422:10 424:13
127:4,9,18	people's 255:5	172:21 174:20	piles 30:12	425:22 432:10
141:10,11	percent 233:22	256:24 270:16	Pira 398:13	448:8 449:18
144:18 145:13	234:14 236:16	313:7 404:14	place 49:12	450:7,21
147:6 148:21	237:17 301:22	Personal 110:11	78:18 84:22	451:23 453:4
163:4 258:21	379:16 380:20	personally	92:14 93:15	453:19 455:6,9
411:10 416:5	385:13,13	266:11 287:23	97:2 153:23	play 304:17
422:9,22 423:7	percentage 41:4	311:21	294:5 358:2	Plaza 4:5
435:16 436:12	Perfect 19:25	pertain 245:8	387:9 459:14	please 14:20
448:5 454:10	38:16	pertaining	471:5	15:24 24:16
464:2	perfectly 332:12	28:13	placed 412:7	78:25 81:2
pelvic 11:18	perform 268:10	pertains 255:20	449:13	83:19 98:12
107:9 427:12	406:17	Peruses 213:13	places 243:15	104:4 113:2,4
428:8 429:7,20	performed 64:4	282:25 300:7	PLACITELLA	113:17 115:14
pending 13:13	74:12,22	308:12 330:17	3:20	122:4 130:17
99:4 242:1	141:17,20	Pervasive	plain 242:21	141:18 156:12
Penninkilampi	149:20 162:6	305:15	plaintiff 165:16	160:15 162:9
237:25 416:11	265:13 403:18	Petta 174:22	171:13 340:15	167:6 169:6
416:24 454:25	perils 302:4	Pettenati 174:23	PLAINTIFFS	211:8,11
Pennsylvania	perineal 11:12	174:25	3:3	214:22 218:10
5:6	76:20,22,25	pharmacologist	plaintiffs' 6:14	219:17 225:21
Pensacola 3:16	211:17 212:21	119:19	7:5 17:14	246:12 318:24
people 41:4	266:22 271:20	phenolics	18:13,20 26:2	325:18 380:12
46:12 63:7,10	278:4 332:24	186:20	28:24 29:12	464:8 466:12
74:8 104:17	359:5 416:8	Philadelphia 5:6	31:13 45:2	472:2,6
105:14 117:3,7	417:11,14	phone 19:21,23	60:23 76:12	plenty 14:16
123:18 142:3	428:6,20	157:24 162:14	133:18 226:5	143:7

pleural 457:25 458:3,4	poorly 338:21	285:13 433:7	214:19,23	270:18 382:23
plot 327:13 348:10,12	popped 423:13	435:1 439:12	216:20 217:9	439:1
plots 327:13	populate 92:21 224:15 345:16	potentially 401:25	218:2 219:8	precise 246:12
plotted 463:9	population 325:10 345:4	powder 1:5 7:4 11:9 13:11	220:11 221:6,6	404:9 450:19
plug 250:15	345:16 356:7	28:14,19 49:3	231:16 233:23	450:24
plus 144:24 420:21	370:7 389:6 405:1	49:20 50:7,13	234:10,12,21	precursor 422:1
PM 370:4	population- 356:16	50:19 51:8,15	236:14 237:15	423:18
pocket 158:23	population-ba... 356:23 357:5,8	52:9 53:4,13	240:17 241:7	predated 423:15
point 42:9 43:24 44:9 57:11	358:14 360:7	53:14,25 54:1	241:10 262:7	predispose 417:20
65:21 93:3	port 460:8	54:18 56:16	263:15,16	predisposition 420:4
99:25 100:5	portions 173:5 173:10	57:13 59:3,11	264:1,2 266:17	predominant 458:9
106:10 163:12	position 71:25 84:15 99:11	60:2 63:23	272:15 273:22	predominantly 374:24
163:17 225:10	153:11 280:18	64:5,25 69:11	274:14 275:2	prefer 344:14
230:4 253:12	314:8 340:5	72:6,18 74:16	276:1 278:22	pregnancy 105:21,22
271:22 277:6,8	370:13 433:25	74:23 75:4	279:2 280:23	106:14,15
314:22 333:3	449:14	76:2 77:12,14	329:6 368:17	pregnant 105:20
340:14 343:12	positions 314:14	77:15 78:3,10	381:19 382:12	premise 344:20
343:22 346:4,6	positive 226:21 270:9 271:19	78:17 79:17	384:5,8,18	preparation 159:18 162:21
346:20 347:8	278:3,15 352:2	80:9,13 84:11	385:12,21,23	180:23 197:12
348:14 350:12	352:16,25	84:16,21 87:17	406:14 407:8	202:7
352:24 373:10	353:4 359:23	89:15,18,19,22	410:22 411:5	prepare 20:5
374:1,16	394:25 417:11	89:24 109:21	411:10,22	129:21 158:4
455:10 458:23	465:15 466:1	111:2,9 120:21	413:9 414:15	180:13,19
462:10	466:19	126:9,14	414:17 415:4,8	185:19 186:24
pointed 350:4	possibilities 395:11	127:11 128:17	415:15,21,23	197:24
pointing 332:6	possibility 396:5 444:21	129:3,13,25	435:17 436:13	prepared 8:5
points 238:2 360:15	possible 12:4 22:8 51:1 63:8	130:25 131:15	451:24 453:5	18:13 27:19
polarizing 11:16 427:10	144:22 256:21	132:7 134:15	460:11,25	29:12 91:10
policy 8:7 84:10 88:11 224:16	285:20 442:20	134:19 135:5	462:19 464:4	92:10 111:17
231:14 235:24	possibly 387:24	135:14 136:7	powder/ovarian 163:3	124:9 129:12
306:2 368:4	post 23:1 29:12	136:21 137:2	power 342:20	129:25 130:25
pollutant 107:25	post-medical 95:1	137:20 138:9	practical 303:25 304:21	131:9,10 132:6
pollutants 102:13,18,23	posture 320:7	140:22 142:12	practice 61:1 63:16 103:17	134:14,18
107:21 108:1,6	potent 221:23	142:16 148:16	106:19 182:10	155:17 156:4
pollution 376:2	potential 59:2	149:22 150:20	307:11 317:14	162:3 171:15
pooled 366:22 368:21 379:14		151:4 163:7,13	317:18	171:25 172:3
379:15 380:19		163:18 164:12	Practices 1:6 13:12	172:13 196:25
383:12		165:25 167:3	practitioner 118:16	197:6 198:18
		167:12 187:6	Pre-School 10:17	201:8 205:8
		199:1,12,25	preamble 425:3	235:23
		200:4,10,22	preceded 270:11	prepares 24:20
		201:3,9,23		
		202:21 203:1		
		209:18 210:23		
		211:17 212:21		

preparing 22:25 23:17 29:19 43:24 202:25 257:19 407:20 421:24 prescribes 63:5 presence 64:25 72:5 75:24 77:1 89:17,21 273:1 384:4 385:20 present 5:22 17:22 19:24 71:5 75:25 76:13 133:23 238:10 282:14 286:12 409:5 417:5,10 presented 29:13 117:19 presenting 70:17 245:15 presiding 219:4 pretty 24:18 46:5 48:14 104:18 106:25 182:5 195:20 217:1 220:5 221:23,23 238:25 286:24 287:12 293:17 303:3,12 315:4 427:1 460:24 prevent 187:12 preventive 47:1 previous 285:16 previously 182:2 186:3 417:16 418:4 431:21 primarily 106:19 142:25 143:24 primary 117:24 117:25 118:8 118:14 124:13 145:20	primates 253:8 prime 315:19 Princeton 4:21 principle 270:13 printer 394:14 prior 18:3 43:24 56:6 150:17 236:6 257:19 264:5 286:1 298:7 334:25 429:15 432:5 437:4 private 429:15 privilege 33:9 33:10 156:20 161:25 166:5,7 166:13 177:11 privileged 176:19,25 probably 14:12 20:15 67:8 92:2 94:9 95:25 104:6 113:21 121:13 158:23 167:19 198:10 202:16 202:18 203:17 207:19 240:17 299:7 310:24 311:5 361:7 392:22 410:14 424:8 434:20 450:15 456:1 problem 58:20 104:7,11 105:9 106:3 107:10 133:3 285:22 301:6 305:16 424:6 problematic 102:17 problems 54:20 procedure 283:12 404:13 procedure-rel... 143:14 proceed 19:18	proceeding 468:10 471:4 proceedings 19:12 44:17 process 14:17 203:23 244:24 261:4 266:4,8 432:11 433:23 455:15 468:1 PROCTOR 3:14 produce 260:15 260:17 produced 26:10 26:14 370:15 product 33:8,12 33:16 49:13 50:19 51:17 53:17 54:17,23 56:16,18 57:5 72:18 74:12 78:18 79:20 84:7,23 87:24 111:9 137:2 171:8 173:19 176:16 180:6 183:22 274:14 382:11,12,13 382:24 383:5 383:12,13 384:18,23 385:21 407:22 products 1:5,7 8:9 13:11,12 49:3 50:7,14 59:3,11 60:2 63:23 64:5,25 69:11 72:6,18 74:23 75:4 76:2 77:2 78:4 78:10,17 79:17 80:9,14 84:6 84:12,17,21 89:15,18,19,22 89:24 110:11 111:2 120:21 126:9,14	127:11 128:17 129:3,13,25 131:1,15 132:7 134:15,19 135:5,10,15 136:7 137:20 140:22 142:12 142:16 148:16 149:11,22 150:20 151:5 163:19 164:12 165:25 167:3 167:13 187:7 199:12 200:1,4 201:9,24 203:1 209:18 211:17 211:18 231:16 231:17 233:24 234:10,13,21 235:25 236:15 237:15 261:15 262:7 266:19 272:15 273:22 275:2 276:1 279:2 368:17 369:8 383:1 384:6,8 385:23 406:14 407:8 410:23 411:10 411:23 415:8 415:22,23 416:6 436:13 451:24 453:5 460:11 462:19 464:4 profession 34:14 professional 171:8 183:21 183:23 203:10 251:10 professionals 462:3 professor 7:15 34:17 93:6,20 94:6,10,13,14 94:15 100:18 profile 103:16	103:20 profound 460:24 program 47:19 48:16,21,23,24 105:18 230:13 262:4,6,9 programs 46:21 47:1,2,2 48:6 367:15,20,23 368:2 progress 135:8 135:14 451:1 project 153:3,7 155:7 191:16 194:7 230:8,10 projects 156:7 187:3,6,9 promise 124:11 promote 317:14 317:15 418:11 promoted 93:6,7 promoting 421:5 promotion 93:5 proof 433:6 446:19,24,25 447:3,5 proofread 176:8 proper 271:3 322:5 323:17 properly 326:10 proportion 41:8 propose 452:10 proposed 417:16 418:4 451:23 proposition 226:23 227:15 306:12 307:14 propounded 18:2 474:6 prospects 39:18 40:15 prostaglandins 444:20 protect 156:16
---	--	--	--	--

protective 285:18 421:21 421:22	107:14 141:11 231:15 235:24 267:2 369:24 370:3 474:19	PubMed 92:16 92:17 108:20 121:17	252:16 267:24 268:6 286:17 310:15 324:16 327:12 368:4 390:17 462:16	251:23 257:17 quantified 371:4 quarrel 278:25 279:5,7,10
protein 423:13 protocol 38:19 160:24	publication 123:24 245:14 321:3	pull 18:16 29:21 69:17,17 339:14 363:4 416:17	Pursuant 2:16 push 306:24 pushing 155:23 put 19:17 29:20 30:1,2 35:12 41:22 45:14,16 52:24 58:6 67:21 83:12 86:7,8 97:25 100:12 165:17 169:18 170:14 172:6,7,8,21 175:19 211:1,4 212:8 215:25 216:3 236:7 254:8,9 267:2 271:11 291:19 299:19 309:11 311:13 326:2,3 327:19 328:12 334:12 336:14 340:23 341:13 346:11,13 355:5,11 364:4 365:9 426:25 438:2	query 404:10,11 question 14:20 14:22 23:20 24:12 28:15 32:4,21 33:10 33:15,18,22 36:11,12 37:22 39:7,20 40:1 40:12 41:16 42:12 47:7,9,9 47:23 49:6,18 49:22 50:25 55:1,13,21 56:20,24 57:9 61:16,21 62:6 62:12,20 64:12 65:16 66:19 68:1,4,17 72:9 72:22 73:4,8 73:12,16 78:24 79:6,11,16 80:17,21,22 82:2 83:18 84:5,9,14,20 85:1 90:2,11 96:18 98:8,11 98:13 99:4 103:22 106:7 106:11 107:17 109:11 112:14 113:3 114:23 115:12 116:23 118:3,14 123:20 124:2 125:3 127:14 132:18,20 133:8,9 135:24 137:11 139:20 144:2 145:17 149:1,13 159:4 161:8 164:10 166:2,20 167:6 168:20 169:5,8
prove 446:1,3 446:10,12,13 proved 419:5,12 proven 445:10 445:15,20 450:7 451:8,16 provide 18:23 37:12 55:25 61:6 62:2 63:8 89:18,22 109:17 180:18 187:24 228:5 316:8 343:23 445:21 460:16 469:13 provided 17:7 17:13 71:4 74:11 88:16 115:22 116:5 116:10,11,12 116:13,24 117:18 118:8 134:24 139:23 157:18,21 165:14 167:2 167:23 172:10 180:12 184:10 187:19 189:12 194:24 207:13 provides 63:5 providing 32:5 183:11 184:7 227:24 provoke 102:12 107:15 public 2:17 8:8 10:13 46:21,25 47:18,20 48:6 48:15,23,25 95:2,6 100:22 101:21,25	publications 121:2,11,15 122:8 123:21 124:9,16,17 125:6,17 126:18 127:4,9 127:17,18 141:10,11 142:23 146:9 245:8,10 454:10 publicly 156:10 publish 143:18 315:13 316:21 317:3 320:9 321:2 published 35:23 45:9 92:1 108:10 121:10 121:16,20 124:4 125:5,11 125:17 126:8 126:13 141:23 142:5,11,15,19 142:25 144:12 144:18 145:5 145:13 147:6 148:21 230:16 236:13 237:14 257:3,25 258:20 259:7 264:22 296:10 319:5,8,18 325:22 359:13 369:2,5 373:8 373:14 381:11 391:7 408:19 411:9 427:19 439:3 461:17 463:15	pulled 170:21 172:2 341:17 pulmonary 34:18,22 52:15 57:3 63:11,17 93:21,22 94:17 94:18 96:9,10 96:10,11 97:17 101:10 103:5 104:16,18,19 104:22 106:20 143:5 153:13 201:6,10,18 205:9 pulmonologist 61:8,17,23,24 61:25 106:4 pulmonology 118:22 188:25 purchased 50:6 53:1,4 Purdie 42:6,16 43:14,15,18 45:7,18 351:11 purported 462:21 purpose 43:22 97:12 162:2 252:21 purposes 18:18 22:4 43:19 55:6 56:16 70:16,24 71:3 71:15 78:9 79:16 93:5 111:16,17 168:1 175:18 183:14 188:3 194:21 242:12 251:12 252:2	Q qualifications 212:17 306:20 442:8 qualify 90:3 qualitative 271:25 273:13 273:14 370:21 quality 144:8,8 149:10 239:14	

170:1,12 172:3 173:22 174:9 176:17 177:2 177:10 184:19 187:13,21 188:19 191:6 191:24 192:5 192:21 193:2,3 199:8 200:2 210:14,16,19 210:20 215:17 217:19,21,24 218:7 219:6,12 220:8,11,14,18 220:21 221:15 221:20 222:9 223:1 224:1 225:3 230:20 231:20 233:15 234:18,22 241:24 242:1 243:10 244:12 252:11 254:18 258:13,17,19 260:6 261:16 265:21 273:18 274:9,11,24 275:7,19 276:2 276:4,9,12 278:7 279:14 279:16 286:5,8 288:5,7 290:25 291:3 299:1 304:16 310:7 319:20,22 321:11 330:7,8 332:4,13 335:2 335:8,11,15,17 335:19,21,22 337:17,20 338:3 339:20 340:4 342:12 353:12 354:1 364:20 371:21 372:7 374:14 375:21 382:16 384:10 385:6	385:16 390:21 391:5 400:12 401:11,15 402:11 403:10 404:5 405:14 406:22 407:11 407:23 408:8 410:20 411:2 412:20 413:15 422:15,19 424:23 427:23 436:10 444:12 446:23 450:15 456:22 457:20 460:21,22 465:4,6 466:15 questionable 256:13 437:2 questioner 19:18 questioning 80:25 83:22 165:19 questionnaire 404:15 questions 27:5 27:12 32:10 37:18 38:25 53:3 82:12,18 83:4,16 86:1 114:8,24 121:25 132:20 154:6 163:10 203:4,23 207:22 210:9 217:20 218:25 254:24 300:2,4 300:9,22 304:5 321:12 326:14 329:23 336:3 346:22 400:3 408:5 430:21 430:24 431:2 435:25 438:19 439:19 440:14 440:20 456:22 467:23 470:11	474:5 quibble 221:8 quick 44:5 293:14 320:16 320:17 377:4,8 399:25 426:10 467:23 quickly 112:1 151:15 quit 218:10 quite 90:6 434:20 451:3 quote 29:21 30:2 425:24 quotes 169:22 170:12 <hr/> R R 3:1 13:1 473:2 473:2 rabbits 253:8 race 236:19 346:18 radiation 115:18 125:23 radiolabeled 412:10 radiologist 119:13 radiology 143:14 RAFFERTY 3:14 raise 80:5 raised 396:13 raising 113:14 113:19 115:2 range 375:18 ranges 105:4 458:14 rank 93:6 ranked 36:2,3 36:16 ranks 34:24 35:5 rarely 352:20 rate 23:11,13	24:2,6,21,22 25:17 178:20 rates 215:8 226:12 ratio 333:11 347:8,16 349:9 349:24 361:4 365:12 368:21 ratios 349:15 351:12 rats 253:8 reach 184:15 190:15 191:15 194:15 195:13 228:16 233:9 279:21 282:12 283:9 314:24 323:13 418:17 reached 155:10 185:21 187:1 193:9,17,24 194:23 227:25 228:6,11 396:10 401:1 reaches 189:7 190:21 191:19 194:8 read 42:16 45:22,23 65:18 66:23 68:8,19 68:20 69:3,6 70:10 72:14,14 76:20 77:3 83:5,11,17 85:24 88:1 97:18 99:25 100:25 101:12 102:24 103:9 111:25 143:11 166:23 181:24 211:8 212:5 214:22 225:20 225:21 231:22 232:21 236:21 239:2 256:21 257:3,21,22 258:20 259:16	259:18,18,22 259:24 260:1 265:6,8,10,15 266:8 270:23 271:15 272:1,6 273:12 277:23 278:14 279:16 282:17 286:6 292:17,22 296:3 298:3,7 299:10 300:18 301:14,17 302:8,15 303:4 304:4 305:6,12 306:3 311:14 311:17 312:1 313:5,14,20 316:15 317:16 348:1 370:9 373:23,25 378:8,10 379:1 379:20 388:14 389:24,25 390:6 395:17 401:18 413:4 413:16 417:21 420:6 423:22 423:22 424:19 425:13 428:3 428:11 429:2 430:9 431:22 439:14 441:7 445:5 448:5 453:15 454:14 462:17 472:2 474:3 readable 469:10 reader 245:23 248:5,11 249:9 249:14,22 250:4,18 reading 28:1 69:1 76:18 79:9 85:15 87:6 198:2 253:24 287:7 291:16 313:13
---	--	--	---	---

389:2 400:5	39:25 70:6	33:22 37:24	152:1 238:21	regarding 31:24
409:24 420:14	185:21 192:24	38:8 44:14,16	244:18 468:21	32:11,14 76:16
469:20	213:16 222:11	44:19 52:24	referenced	124:17 127:10
readings 128:3	223:10 272:19	53:16,24 54:3	397:14	127:19 173:20
reads 96:8 101:7	315:8 341:5	58:5,10 83:22	references 66:10	295:16
198:14	407:4 409:20	89:4,7 99:11	171:6 364:19	regardless
ready 44:22	410:10 412:6	115:13 132:2	396:20	280:25 322:11
315:19 377:19	462:1 472:4	134:7 151:17	referrals 104:19	379:13
real 44:5 133:3	473:6,8,10,12	151:20 154:13	referred 118:22	region 11:19
301:5 316:2,3	473:14,16,18	204:20,23	118:24 120:3	427:12
316:4,5,6,7	473:20,22,24	234:6 280:11	referring 28:23	regional 428:9
399:25	reasonable	280:14 320:19	43:1 65:5	429:8,20
realistic 270:12	79:19 87:19	320:22 324:23	237:7 255:24	Registry 8:12
realistically	445:8	331:23 336:16	282:6 292:7	regret 44:8
462:11	reasons 332:18	338:5,7,14,15	297:7,10,25	regulatory
reality 229:4	361:7 384:12	338:17,24	298:21,25	56:14 119:21
383:8,18,25	REATH 5:4	344:11 350:15	389:22 441:1	209:1 434:12
realize 27:15	recall 41:23	377:10,13,14	refill 88:20	Reid 388:3,15
99:22	67:12 146:3	377:15 378:19	reflect 53:24	388:18,19
really 21:6 53:7	176:4 197:2,10	393:3 426:17	97:20 101:14	389:3,12
53:7 68:13	389:2,7 402:12	426:20 431:8	113:18 115:13	390:10,11,12
70:10 77:17	465:6,11	440:10,24	179:13 344:12	390:12,13,18
93:7,17 105:3	recalled 270:10	441:8 447:8,11	349:9	Reids 390:11
114:10 133:15	receipt 472:13	447:14 464:11	reflected 69:12	reiterating
149:10,10	receive 102:2	464:13,16,20	Reform 231:13	403:13
180:10 191:23	received 20:17	464:21,23	refresh 65:20	relate 187:14
201:21 210:21	21:16 95:2	467:18 470:17	380:10	405:20
221:13 229:15	148:9,12,15	recording	refusing 33:21	related 33:4
231:6 237:6	175:23 229:20	173:6 242:10	regard 14:5,11	121:22 123:23
240:10 252:21	468:14	recorded 471:8	31:17 33:18	142:2 143:22
258:19 269:15	receiving 187:18	records 30:4	35:6 49:18	199:4 200:8,10
293:10 295:10	469:5	167:21,22	57:3,11,21	200:12 201:4
310:4 331:24	recess 89:5	177:13	60:1 76:2	257:17 285:22
332:17 334:4,4	151:18 204:21	Red 3:22	84:11 96:16	380:2
335:8 340:24	280:12 320:20	redacted 161:24	120:10 126:14	relates 1:10
344:20 353:18	377:11 426:18	180:5	129:6 157:12	403:9
358:13 360:11	447:12 464:14	reduce 32:19	159:18 175:24	relationship
364:3 374:4	recognize 78:13	46:22 172:9,23	176:13 177:7	127:11,19
382:6 405:24	239:9 361:12	367:15,23	225:14,15	153:20 154:17
420:24 422:4	467:3	368:2	233:10 251:11	157:5 200:16
423:16 425:4	recommenda...	redundancy	256:15 280:18	210:22 212:20
462:9 469:8	406:16 407:2	74:6	287:15 310:16	273:21 274:13
realtime 300:21	record 13:4,19	redundant	315:25 356:7	275:1 376:9
345:11 450:16	18:18 19:8,11	245:14 247:12	370:17,23	379:10 463:11
reanalysis	19:14,16 26:10	Reeds 388:16	373:14 381:18	relationships
388:25	27:6 28:22	refer 265:18	384:19 409:2	358:1
reason 21:11	31:7 32:16	reference 66:2	434:1 441:11	relative 9:19

Gregory B. Diette, M.D.

Page 520

327:18 328:9	32:21 36:2	94:10 111:17	255:23 256:1	70:6 71:19
328:18 329:5	53:23 60:20	129:12,14,21	256:11,18	129:24 130:4
332:14 336:9	63:19 69:3,7	129:21 130:8	257:10,20	131:9 134:18
339:2,15,23	69:15 138:11	130:21 131:4	258:1,11	156:4 162:16
340:9 342:4,6	144:24 145:2	131:20,22,23	264:10,14	165:15,20
343:15,16	152:25 153:5	132:5,8,10,14	267:6 268:7	175:3 180:16
348:13 349:11	158:3 161:8,9	133:24 134:7,9	315:12 324:4,5	180:19 185:19
352:1,16	164:4,17 171:4	134:13,25	325:5 326:1	186:4 202:8,25
353:10 360:20	182:8 197:14	135:1,13	327:12 332:16	203:4 239:4
361:15 363:24	197:22 231:22	138:17 145:25	334:3 336:1,5	257:9 297:11
365:4,5,17	242:22 247:10	152:3 153:16	336:19,23	329:5 374:7
366:19,22	252:19 253:6,8	154:24 155:12	341:13 346:21	407:21 417:10
367:16,21	265:9 283:17	155:17 158:5	355:22 356:4	453:18 454:4,5
368:16 370:17	288:17 296:8	159:19 162:3	356:13,13	repository 92:20
370:25 371:11	296:12 311:21	162:22 163:21	357:17 360:4	represent 18:19
371:12,16,23	380:6,7 389:11	163:21 165:7	360:12,16	18:21 28:17,18
372:11,22	392:17 395:24	168:2,18	364:23 366:19	40:8 45:3,4
373:16,18,20	425:2,6 426:1	169:11,12,17	367:2 378:4,7	52:7,24 53:3
374:7,23 375:7	426:7 432:17	170:4,10,14,14	378:25 379:8	55:14 81:12,15
375:18 377:25	460:4,6 463:21	171:12 172:5	390:18 393:4	84:2 98:3
379:16,23	468:2,14	172:12 173:5	395:19 396:13	101:19 103:11
383:3 387:17	remind 113:7	173:11,16,21	397:15 399:16	103:13 108:14
397:25 398:10	160:5	174:4,10	408:18 421:24	139:11 224:23
398:14,21,23	reminded	175:19,24	421:25 432:9	225:9 232:10
399:10 400:5,7	455:13	176:1,14,24	443:21 447:21	235:21 236:5
relatively	reminds 68:24	177:8 180:13	460:5,8,16	289:25 291:20
343:23	removed 280:22	181:13 182:22	468:2,5,10,20	292:8 297:21
relevance	render 256:13	183:15 184:9	469:15,18,23	308:14 312:5
315:25 342:6	rendered 161:13	186:24 193:12	470:7	317:1 325:23
relevant 145:22	repeated 420:1	198:6,9 201:8	reported 1:25	325:24 327:9
211:15 238:13	repeatedly	203:21,24	9:21 270:11	327:17 343:11
reliable 416:4	461:23	205:4,6,7,7,16	291:5 337:2	350:14 364:12
reliance 34:5	rephrase 408:6	206:14,14	339:6,9 371:14	387:4 397:13
43:2,7,9,10	422:19	208:9,23	372:11 375:6	399:12 438:8
65:21 165:18	replace 309:7	209:24 210:4,8	428:20 463:19	438:25 442:19
388:15 468:23	replacement	210:25 212:2	reporter 2:17	representation
relied 65:18	315:16	227:25 228:6	13:19 188:9	54:4 324:23
381:24 440:17	report 6:19 7:16	232:21 233:8	279:12 440:21	representative
rely 71:9,21	10:21 21:12	235:13 237:2	471:1,2,24	84:15 86:9
72:1 166:15	22:5 29:19	238:11 242:12	reporter's	represented
233:3 255:10	30:8,11 42:6	242:16,23	471:13	242:15 339:24
381:23 390:18	42:14,22,24	243:11,23	reporting	386:8 387:4
relying 68:14	43:7,24 66:4	244:7 248:15	247:13 270:9	representing
70:18,25 71:6	66:10,23 67:14	248:18,22	reports 20:14,15	55:18 221:1
71:10,17 167:5	68:8,19 70:21	249:3,8,21	21:5,20 22:11	223:14
remember	70:25 71:4,7	250:3,17	60:6,12 66:18	represents
22:10 27:22	75:24 76:4	253:17 255:19	67:4,21 69:12	17:25 18:5

Gregory B. Diette, M.D.

Page 521

21:15 28:7	202:4 230:8,13	rest 237:18	455:14 462:15	40:24 41:1,5
81:24 224:7	242:19 262:6	244:13 414:21	463:8	42:2,4 44:1
327:11 382:9	262:10,12,15	420:14	reviewed 6:22	45:12,24 46:4
reproduced	294:14 298:15	result 305:25	19:5 20:5,6	46:7,10,17
26:16	306:1 308:17	352:2 382:14	42:5,6,15	47:10 49:3,17
reproduction	309:21 310:12	resulting 413:9	43:21,23 59:7	50:6,18 54:10
439:4,6 471:22	313:11 314:19	results 69:10	59:24 65:18	58:1,13,16,18
reproductive	319:7,15,24	70:18 71:18	66:3,8 77:9	58:23,24 61:10
36:7,15 61:2	367:10 369:13	256:13 287:3	80:18 82:13	61:25 62:7
reputation	369:14 403:3	291:5,7 292:14	83:16 111:16	63:16,20 65:10
230:4	444:24	292:15 293:6,9	121:21 124:15	66:15 67:11
request 16:24	researched	366:24 395:20	157:21 244:18	70:3 71:21,22
18:20,21 26:11	119:6	407:25	245:1 246:8	72:4 73:11,23
26:17 31:3,15	researcher	retain 194:15,20	247:2 250:19	74:6,10 75:19
31:24 32:25	34:16 224:13	retained 7:5	251:11 257:23	77:5 78:15,16
97:1 99:15	researchers	51:5 55:5,13	357:17 373:13	79:24 80:1,2
164:6 192:16	215:6 225:22	108:21 109:16	374:6 378:24	80:12 81:4,6
426:2	226:4 295:16	136:6,6,25	381:16 409:9	82:6 88:3,12
requested	309:14 310:1	139:13 140:21	412:15 438:17	88:13,15 89:14
155:11 199:13	researching	150:18 151:2	448:25 451:22	90:4,8 91:23
231:25	233:8	171:13 195:1	452:17 459:23	92:5,9,12 94:2
requests 6:15	resembles	208:24 228:5	460:3	94:5,14,16
17:15 18:1,6	268:15	242:4	reviewers	95:17,20 96:2
32:1,14 33:7	residency 117:6	retainer 31:20	319:10	96:5,8,15
require 251:10	117:9,12	retention 56:12	reviewing 30:6	97:13 99:4
required 315:12	resisted 273:16	Retire 9:4,12	37:11 67:13	100:17 101:14
362:9 457:18	361:10	retrograde	185:8 407:5	101:17,24
reread 67:6	resonate 215:20	273:3	RICE 4:10	102:10 103:11
rereviewed	215:23	return 472:11	Richard 4:18	103:16 106:18
259:5	resonates	reveal 173:19	11:25 438:9	108:21 110:9
Res 369:11	215:22 216:4	review 10:12,25	rid 311:14,16	110:22 114:8
research 9:8	217:5	11:14 17:3	ridiculous	116:21 119:13
48:24 97:14,21	resources 311:1	19:2 20:21	270:16	120:13,23,24
101:8,15	respect 67:19	39:15 42:4	right 14:9,18	121:1,14
102:11 103:2	respected 260:9	43:18 55:22	15:1,5,8,9,15	122:23,25
103:12 107:13	260:13	60:11 82:18	15:23 16:22	123:10 124:4,8
108:3 121:2	respiratory	83:3 148:22	17:2,5,7,24	124:14 125:5
128:16,20,25	142:3	149:6,9 153:4	18:9,11 20:3	128:1,19
129:2,5 143:1	respond 32:16	154:1 189:9	20:18 21:1,11	130:15 132:11
143:13 145:20	114:17	190:2 212:17	21:19 22:2,10	132:23 134:6
146:8 147:17	response 6:14	222:20 240:2,7	22:16 23:4,10	134:12 135:10
147:22 148:5	17:14 18:12,20	241:16 242:24	24:1 26:6,25	135:25 136:18
149:12,14,17	26:11 28:24	244:15 253:15	27:21 30:1,9	139:1,15,21
149:21 150:19	32:25 417:19	256:10 264:22	30:19 31:1,10	140:13,16,19
151:3 162:20	418:7 440:4	264:24 380:25	31:15,20 33:13	141:2,4,9,22
163:4,22,24	465:18	411:22 422:8	34:13 36:5,19	142:5,10
164:11 190:17	responses 18:1	427:20 448:4	37:5,8 39:14	144:15 145:2

145:12,19	276:24 278:16	389:24 390:17	126:14 172:23	423:9 446:15
149:13 150:24	280:2,21 282:5	391:22 393:9	214:6,6,16,24	451:18 466:8
151:8,22,24	282:8,19 284:2	393:18,25	215:4,5 216:21	466:23
152:3 154:9	284:15 285:1,5	394:7,8,15,19	217:10 218:3	risks 235:25
155:13 157:3	286:15 287:12	394:22 396:18	219:8,24 220:1	327:18 336:9
157:15,19,24	288:15 289:6	397:22,25	220:12 221:7	337:2 339:2,15
159:2,25	292:7,24	398:17,19	221:16 222:5,6	342:7 360:20
162:10,18	293:19 295:3	399:2,20 401:7	222:18 223:18	361:12 363:24
163:2,17 165:5	296:16,17,17	402:23 405:4	223:19 225:15	365:4 367:16
168:10,17	298:9 299:18	405:18,24	231:15 233:22	367:21 368:12
169:23 170:9	300:24 301:25	407:17 408:17	234:14 236:16	368:16 370:18
170:19 174:17	302:3,20 305:5	408:20 411:8	237:17 238:3	372:11 375:7
177:23,25	305:11 306:16	413:2 415:7	240:18 248:1,1	375:18 379:23
178:6 181:4,18	307:22 308:5	416:22 418:2,3	262:18,23	400:5,7 401:2
182:10 189:18	310:22 312:25	419:21 420:8	263:9,11,13,16	Road 2:6 13:10
189:19 191:2	313:14 314:5	424:8 425:8,19	263:18 269:10	Roberta 442:20
194:13,16	316:3 317:7,24	426:12 427:8	285:13 328:9	ROBINSON 4:4
198:5 203:16	319:1,6 322:25	427:19 428:13	328:18 329:5	role 12:4 48:10
203:20 205:2	323:17 324:11	428:22 429:19	332:14 339:23	117:25 154:21
206:13,18	324:12 327:5	429:21 431:4	339:24 340:9	288:18 294:19
207:6,25 208:6	329:10 330:1	434:6,17,24	342:4 343:15	442:20
208:17 209:11	332:10 333:23	436:24 438:7	343:16,24	roll 38:7
210:7,14,24	333:24 334:2	440:12 442:4	348:13 349:11	Roman 276:15
211:21,23	338:7 340:25	448:20 449:11	352:1,16,16	Ron 309:7
213:24 214:5	343:2 344:9,22	454:11,17	353:10 359:14	room 353:2
214:10,22	344:25 345:3,9	455:10 456:5	359:23 361:4,4	ROSEN 3:5
215:11 216:9	347:11 348:16	456:21 458:23	361:13,14,15	52:5 85:19
216:18 218:20	349:14 350:2,4	460:13 461:4	361:15 362:15	86:13 139:6
218:20,22	352:7,18	462:22 465:13	362:17 364:11	393:3,9 427:4
222:20 224:5	353:17,19	465:17 466:8	365:5,17 366:2	437:21,24
225:5,25	354:8,18 355:1	466:17	366:19,22	Rosenblatt
226:17,17	355:5,16,19	right-hand	368:15 370:25	351:13,23
227:5,6,20,20	356:10 357:2,7	327:14 419:13	371:11,12,16	rotate 117:7
228:4,25 232:5	358:12,17,23	Rigler 65:11	371:23 372:18	ROTH 3:20
236:23 237:5	359:15,18	66:6,11,15,24	372:23,25	Rothman 8:20
239:18 242:6	361:16 362:6	67:14 68:9	373:16,18,20	287:21 290:9
242:15 247:21	362:13 363:3	70:25 71:8,18	374:7,8,15,23	292:9 317:13
253:22 254:4	365:24,25	72:5,15,16	376:6 377:25	322:11 361:2
254:24 255:13	366:16,25	Rigler's 69:10	379:17,17	456:2,3 463:8
256:20 257:19	367:5 369:7	70:19	380:20 383:3	463:8,16
258:25 261:18	370:16 371:3,5	rings 303:9	387:17,20,20	Rothman's
264:19 267:5	375:5 376:14	rise 387:24	389:5 398:1,10	288:8
267:14,23	378:14,22	risk 6:23 7:23	398:14,21,23	roughly 376:23
268:24 269:7	379:6 380:1	8:8 9:20 10:5,9	399:10 402:1	route 284:21
269:20 271:2,9	383:9 384:17	45:8 59:2,10	411:5 413:11	285:7 413:11
271:12 272:23	385:10 386:10	79:8,10,15	414:17 417:15	row 333:6
273:6 275:8	387:2,20	80:5 125:12,18	421:18 422:23	rows 334:12

RPR 471:18	sat 179:9 338:23	277:22 278:22	168:3,17	screen 13:7
RR 350:25	saw 60:19,21	284:2,2,3,17	170:24 175:14	85:24 378:17
351:1 367:3	65:10 69:17	300:25 302:3	178:22 179:7	Screening 8:11
RRs 336:7	94:9 182:11	302:21,21	179:14 188:20	se 30:21 48:24
rubbing 154:13	230:1 231:20	331:10,15	189:7 190:15	65:3 185:2
rule 251:19	257:8 296:8,9	340:17 365:15	190:19,20	195:1 425:12
315:11 361:23	299:4 307:3	369:23 386:14	223:22,22	search 92:17
362:3	311:4,22	393:25 394:19	264:23 315:3	147:4,11 164:3
ruled 396:4	312:23 313:22	397:16 401:20	317:8 381:25	164:18,20
ruler 353:21	314:16 409:2,6	417:5 419:24	468:8	240:1,8,22,24
rules 160:20	421:24 429:22	428:6 429:19	Sciences 32:11	241:1,4,8,17
166:6 316:19	saying 37:2 40:7	437:23 439:24	32:15	242:2,7 313:6
317:4,9,11,12	53:14 82:25	scale 353:17,19	scientific 30:7	searched 246:21
run 208:17	146:3 164:5	361:17	30:10 31:11	searches 162:24
237:22 314:21	182:13 189:24	scanning 11:17	35:24 37:11	238:21,22
353:21	191:5 219:15	427:11	39:15 42:18	240:5 241:19
running 437:17	220:2,8 224:6	scenario 193:14	56:17 57:12	sec 282:22
	224:22,22	194:4,5	59:25 70:13	sec- 100:7
S	227:1,10	schedule 158:2	120:9 146:8	second 19:8
S 3:1 6:1,8 7:1	237:13 243:18	Schildkraut	162:20 176:13	44:14 66:1,9
8:1 9:1 10:1	251:19 277:4	351:14 413:4,8	177:7 189:9	96:24 97:13
11:1 12:1 13:1	279:6 295:1	413:20 436:4,5	209:1 212:18	100:7 198:10
Saed 255:21	305:2 311:17	scholar 242:20	222:21,22	214:12,16
256:2,15 257:4	330:1 334:2,3	242:20 244:18	228:7 229:21	225:19 274:22
Saed's 256:10	351:20 359:8	school 95:1,21	234:11 257:3	290:12 321:14
256:11 257:21	365:12 368:11	95:25 96:4	260:4,9 291:4	330:15 350:15
257:22 258:20	372:16 374:14	100:19,21	291:6 295:19	351:3 363:18
safe 46:5 407:22	383:16,24	101:21,25	303:25 304:21	366:7
safety 84:7	385:4 387:19	117:5 215:3	319:17 342:14	secondhand
234:10	424:5 449:18	222:4 223:17	360:25 374:6	10:5,11 102:14
salad 268:25	450:12 455:2	294:8	375:7 407:24	107:22 363:20
269:4,5	456:15 460:4	schools 223:16	411:9 416:4	363:22,24
sales 1:6 13:12	says 23:12 49:9	science 24:19	436:12,24	364:1,10
327:11	50:20 54:18	25:18 31:18,21	437:1 448:5	365:14,23
saliva 404:25	55:3 66:10,16	31:25 32:6	453:15	366:3,20
406:3	76:11 84:1	33:3,5,20 34:2	scientist 58:25	367:10,16,23
sample 248:25	85:9 95:23	56:14 151:23	120:4 230:18	368:2 371:13
249:2 316:8,10	96:25 97:13	152:5,10,18,22	231:2 289:1,12	376:14 377:25
341:7,11,16	100:14 102:6	153:15 154:8	450:18	379:10,13,18
342:2,13,16,23	102:11 103:7	154:16 155:10	scientists 59:23	380:2,21 393:8
Samuel 11:20	113:7 114:3	155:16,18	60:13 222:22	402:14,19
Sander 288:22	121:10 189:7	156:5 157:4,8	223:4,6 295:16	403:3,6,9,14
289:1 290:12	191:7 206:14	158:10 159:7	306:23 307:19	403:22 405:11
297:21 317:13	207:16 214:19	161:12 162:5	307:20 310:13	secretary
sanitary 331:14	216:16 219:5	162:19 163:21	389:3	176:23
332:21,23	220:9 273:12	164:10 165:5	scolding 301:3	section 92:3
334:17,22	276:8,18 277:9	165:21 166:25	scoring 250:18	176:7 243:20

243:22 244:14	327:15 328:6	111:9,21	57:6,9 72:1	162:5,17
268:13 278:12	328:10,14,17	205:25 213:12	91:14 112:1	180:18,22
282:9 305:15	328:20 329:2,4	213:17 214:1	207:20 239:5	189:12
357:22 366:19	329:8 330:13	222:21 226:5	283:16 341:14	services 11:22
416:23	332:22 336:24	238:3 258:6	361:21 388:10	13:5 117:7
sections 181:21	344:23 345:1	259:19 281:9	390:16 403:1	154:19 161:13
see 16:22,25	353:24 355:13	281:10 299:21	415:2 447:23	180:12,24
23:7 26:4,7	359:4,7,24	300:12 304:13	451:1 460:7	181:7 186:23
37:4 42:6	364:17,22,25	311:6 320:6,7	462:7	187:18,19,24
44:12 45:10	365:3,7,15	320:25 329:24	sent 67:19,22	192:15 194:6
50:20 54:11	367:4 375:22	367:17 368:17	153:4 161:23	194:24 195:23
58:7,19 59:13	388:15 391:11	376:7 386:12	sentence 46:7,15	197:21
63:7,10 66:5,6	392:20 394:19	386:13 387:22	92:24 211:9	set 24:14 44:3
66:12,13,15,25	395:3,7,15	391:6 411:19	212:14,15	47:1 86:24
67:9 69:6	396:1,7,9,20	411:21 412:2	215:1 223:13	89:13 145:14
74:22 79:14	396:21 397:20	412:15 413:3	227:18 235:14	157:24 205:15
81:4 96:5,6	397:25 398:3,6	415:12,17	276:7,18,20	231:10 243:11
100:1 102:3,10	398:9,14,19,25	416:11 422:4,8	278:14 280:1	243:23 286:15
103:17 104:6	399:3,7,8	423:8,12,16	291:24 302:3	291:5 292:13
104:16,17,18	400:24 401:5	427:22 431:24	306:10 323:2	317:11 324:3
104:24 105:9	402:4 409:17	436:2,24 437:1	366:24 372:7	454:19 460:9
105:24 117:3	410:9 413:17	437:8 438:17	374:20 428:5	471:5
118:21 121:18	414:14,19,22	440:7 442:5,13	sentences 182:1	setting 105:13
122:14 123:12	418:22 419:23	442:25 448:25	272:25 306:14	105:14 353:1
124:9,11 134:2	424:12,16	451:21 452:9	separate 110:2	settings 51:11
138:13 143:12	425:19 427:13	452:22 453:2	138:18 241:4	seven 331:11
144:22 148:8	427:17 429:23	453:16 454:1,1	332:24 388:23	345:12 467:13
153:6 157:20	432:23 433:10	454:12 459:14	separately 18:14	severe 287:12
168:5 170:10	436:10 438:6	sees 104:25	136:24 178:18	SEYFARTH
181:20 188:4	438:14 441:5,8	113:21	241:8	5:17
196:15 206:7	441:10,12,14	segment 172:22	separating	Shannon 175:9
213:13 214:8	443:2,8,10,14	select 244:5,25	301:6	shape 91:18
214:11,17,20	443:15,17	333:11 344:3	September	168:23 169:11
218:24 221:3	444:15,25	selected 170:4	11:23 140:3	169:12 170:24
224:24 236:2,3	455:5 456:9	327:11 344:4,5	438:8,25	170:25
236:9 237:23	457:17 462:16	345:4,16	sequence 20:25	shaping 175:24
254:7 270:23	seeing 41:23	selecting 245:24	seriously 434:20	share 22:22
271:12 272:9	105:17 107:7,8	344:12	seriousness	71:16,17
272:11 277:10	108:14 422:3	selection 251:11	133:11	156:25 165:4
283:21 290:3,7	seeks 166:4	261:4 345:21	serous 417:12	185:17 228:1,7
290:10,15,19	seen 16:18,20,20	sell 50:13 79:19	serum 423:13	228:12,18
296:6 297:2,4	35:1,1,23 36:1	80:13 87:19	serve 108:22	242:23 261:22
301:12 302:1	36:1,3 51:10	385:12	served 18:6	309:19 391:1
305:16 309:17	51:12 60:5,8	selling 87:24	203:5 340:13	438:1 441:22
312:1,20	64:23 65:2	send 164:23	service 8:12	shared 75:15
313:21,23	67:3 74:18	senior 370:13	105:2 107:7	208:13,24
315:15,20	83:3 110:22	sense 46:8 56:23	157:18 159:20	209:17 441:20

Sharfenstein 313:1	378:4 shown 215:8	357:20 428:10 significant	447:20 458:16 461:23	366:20 367:11 367:16,23
Sharfstein 313:2 314:9,19	226:12,17,21 415:17 416:10	233:21 234:13 236:16 237:16	sir 141:6 324:13 SIRs 400:8	368:2 371:13 376:14 378:1,7
319:16,23 sharing 71:16	435:24 437:6,8 shows 236:14	237:21 269:13 271:19 278:3	sit 304:14 site 417:13	379:11,13,18 380:2,21 393:8
205:14 212:25 SHAW 5:17	237:14 281:10 281:18 353:10	278:15 285:25 286:21 287:4,5	sitting 15:1,10 68:4 69:9	393:8 402:14 402:20 403:3,6
She'll 385:8 sheet 308:15	423:17 435:22 436:2	291:8,10 292:15,21	121:14 363:10 412:14	403:10,14,22 405:6,11,22
472:5,6,9,11 474:8	sick 104:13 sickest 104:12	293:15 302:13 303:15 305:25	situations 135:22	456:24,24 smoked 404:12
Sheraton 2:5 13:9 15:2	side 60:23 308:20 327:14	309:6 318:11 321:8,9,19,20	six 57:24 319:2 401:3	404:21 smoker 379:19
Shih 421:25 Shih's 421:25	Sidney 7:22 214:3 215:14	322:7,8,19,20 323:10,19,20	size 191:1 248:25 249:2	380:22 smokers 10:6
Shirm 309:8 shopping 50:8	224:24 225:5 225:12 228:16	356:22,24 357:4,11 360:9	316:9,10 341:7 341:11 342:2	364:11 365:13 365:14 366:20
short 19:17 shorten 349:3	Siemiatycki 172:7	365:13 456:8 456:13	342:13,16,23 343:1	366:23 smokey 405:20
426:15 shorthand 471:1	sign 206:22 307:14,24,24	signing 472:8 silica 259:7,12	sizes 341:17 SKADDEN 5:10	SMRs 400:8 snack 204:14
471:2,11 show 17:17 45:1	307:25 472:6 signal 301:7	259:15 similar 64:14	skilled 51:21 52:15	snippet 85:6 snippets 83:22
52:2,20 80:3 95:8 98:22	358:19 359:8 458:25	188:17 245:11 280:24 335:24	sky 380:15 sleep 34:22	97:25 Society 439:5
138:21 139:1 154:13 213:3,6	signatories 311:18 312:6	similarities 285:23 286:9	93:23,25 94:1 slice 237:7	Society's 298:13 sold 75:5
235:16 281:22 289:19 296:17	312:17 313:23 314:6	similarly 49:25 269:18	slightly 400:9 small 271:18	solely 302:11 303:13,14
296:22 311:23 312:4 331:20	signature 208:1 signatures	simple 61:16 62:17 64:21	278:2 282:13 331:16 340:18	soliciting 312:14 somebody 20:20
364:7,9 366:1 390:1 392:24	312:15 signed 264:10	335:20 403:20 simplify 201:7	342:17,23 360:21,21,25	49:9 70:14 83:23 90:21
393:13 396:24 413:20 415:3	306:23 307:21 312:2	421:2 simply 37:12	362:15 363:11 371:7 420:21	97:2,25 104:20 105:19 107:8
431:4,17 432:15 436:6,8	significance 9:5 9:13 286:2,19	57:9 287:19 291:6 292:14	451:17 smaller 205:19	153:3 159:22 160:1,4 173:7
437:12,18 438:7 442:18	295:17 298:14 302:5 303:6	293:10,10 327:19 354:1	361:17 smart 311:12	178:1 185:1 188:16 191:6
462:24 showed 358:4	304:1,22 306:25 309:13	441:1 453:14 456:6	Smith 182:12,13 smoke 10:5,11	196:13,22 224:10,12
463:22 Shower 50:1,2	309:24 310:1 310:17 311:16	Singh 172:8 single 104:7	10:21 102:15 107:22 363:20	240:6 255:6 287:13 293:11
51:8,8,16,16 74:15,15	312:8 314:17 316:1 318:10	246:16 247:9 248:13 363:1	363:22,24 364:1,10 365:4	324:7 340:20 352:24 376:5
showing 9:19	323:5 357:19	371:2 373:9	365:16 366:4	412:23 461:2

somebody's 394:14 465:22	78:14 91:18 92:21 110:8	spaces 174:19	231:4 233:4	started 28:16
someone's 191:17	123:16 130:20	speak 98:6	235:8 261:2	29:4,6 189:17
somewhat 221:18 256:20	144:16 146:15	113:13	314:10 430:8	250:14
soon 93:17	152:13,16	speaker 115:11	435:6	starts 48:25
113:25 205:5	158:1,4 168:25	speaking 64:19	speech 37:17	225:20 236:9
sophisticated 64:15	175:14,15	109:20 115:9	98:7 114:16	292:10 299:20
sorry 23:21	176:10 181:23	142:2 207:3	193:6 442:1	394:9 395:9
26:20 28:4	185:3 195:2	213:15 260:14	speeches 37:24	419:21 432:23
43:3 45:3	211:24 230:7	301:17 326:15	92:13,19 113:3	state 2:17 38:3
48:12 58:19	241:3 252:7	389:14	114:15,15,18	45:19 75:23,23
69:25 76:22	257:11,17	special 9:9	115:14	111:3 112:17
85:3 87:9	266:25 267:3	292:12 301:1	speed 454:16	272:10 414:14
97:10 99:19	268:24 292:19	308:17 309:3,9	spell 423:25	432:2 472:3
112:20 116:12	297:3 313:21	specialist 120:4	spend 152:2	stated 146:1,10
126:23 131:18	332:23 343:5	188:25 254:15	173:15 175:17	255:18 286:18
139:17,19	358:13 382:6	255:14	175:25 177:14	395:19 436:13
171:19 172:14	383:23 392:17	specialties 194:9	183:23	452:17
177:3 188:10	405:3,20 425:2	specialty 260:24	spent 23:5 37:10	statement 8:4
210:20 227:14	425:5 437:5	specific 68:25	408:2	36:10 37:21
237:11 243:17	452:11,13	118:3 123:20	spill 171:3	38:11 46:5,18
258:8,24 260:5	454:21 456:7	131:22 207:1	split 171:5	46:24 77:7
269:3,21	458:14 461:22	207:11 223:3	spoke 168:4	172:25 217:2,4
279:11,12	462:4,13 468:1	252:1 276:7,12	468:12	217:9,14 220:6
283:22 316:4	468:24 469:10	276:17 277:9	spontaneously	221:22,24
324:7 327:3	sorted 242:13	361:11 381:17	126:1	222:7,16
330:3,14	sorts 104:14	specifically 67:7	spur 206:2	224:17 226:1,6
345:10 348:17	143:15 181:16	67:13 83:11	Square 5:5	226:15 235:3
348:22,22	223:9	122:22 123:9	stab 103:20	235:22 236:5
351:19 364:7	sounded 116:16	146:2 182:9	stack 30:9	236:24 238:6
365:23 366:8	199:7	236:7 324:3	staff 171:17,20	246:5 273:8
368:8 370:2	sounds 55:19	331:13 417:12	171:21,23,24	277:9,11
373:4 379:15	88:11 118:14	specificity	172:10,21	278:22 282:20
379:25 386:21	120:13 152:4	270:24	173:1,1 208:18	291:11 292:25
391:20 394:10	164:14 235:12	specified 362:9	stage 39:17	293:17 295:19
397:10,11	258:8 295:11	362:12	40:14 46:23	302:17 303:20
414:4 419:25	301:21 313:17	specimens 422:2	115:8 454:20	304:2 305:3
424:5 425:9	344:13 390:15	spectrum 451:4	stakes 93:2	306:21 420:9
431:19 433:3	445:8 447:1	speculate 444:9	stand 337:4	425:7 432:18
441:12 446:6,6	source 126:19	speculation	standards	432:21 433:16
446:17 450:13	127:5 225:7	60:18 75:11	120:11	436:22 445:2
469:20	369:25 376:1	110:16 157:10	standing 352:14	447:23 452:23
sort 24:3 49:12	sources 370:4	158:15 178:13	standpoint	452:25
64:18 70:7	404:24	178:25 186:11	263:6	statements
	South 3:15	188:6,12	start 28:10 66:3	234:5 293:3
	space 472:4	191:21 194:11	240:4,11	304:18
	spaced 407:16	195:14 196:2	241:11 243:21	states 1:1 13:14
		229:23 230:20	355:1	36:22 97:14

100:17 103:2	stay 299:18	287:18 293:17	286:20 288:11	461:6,18,23
236:12 282:11	355:14	314:23 361:21	293:15 305:24	462:4,5,17,21
303:24 305:18	stenographic	362:22 363:7,7	319:2 321:7,17	462:24 463:23
308:15 309:2	13:19	421:11 452:22	321:18 322:5,6	464:2
367:14 400:25	stenographica...	strongest 392:3	323:9,13,18,25	study 11:11
434:12 439:2	471:9	392:4	324:3 325:6,6	21:23 22:9
444:17	Stewart 350:17	strongly 394:25	325:10,12,13	42:17,17 123:2
statistical 9:4,13	351:4	struck 256:12	325:25 326:13	142:9 144:14
286:19 295:7	stick 421:25	257:11	327:11 332:22	144:19 146:7
295:17,18	sticker 29:20	structure	333:10 334:16	148:10,13,16
298:13,14,17	30:1 86:8	190:14	335:25 336:17	182:2,4,16
303:6 304:1,22	stickies 30:15,16	stuck 275:8	338:24 339:3	183:11 184:8
306:25 309:13	stood 280:19	316:16	339:14 341:7,9	214:25 215:3
309:24,25	stop 133:4	studied 77:14	341:18,19,21	222:4,12,14
310:17 311:16	156:12 305:19	150:6,12	342:1 343:6	223:16 232:25
312:8 314:17	337:11 456:15	370:24 449:1	344:7 345:21	233:11,13,14
315:25 318:10	stops 48:25	453:17 467:9	345:23,25	233:16 245:11
323:5 357:18	store 50:10 53:5	studies 9:17,17	349:8,9,19	247:3,23 248:6
statistically	story 254:11	10:7 11:4	351:24 352:1	248:12 249:15
233:21 234:13	410:13,17	64:22,23 77:2	353:9 354:2	249:22 250:16
236:15 237:16	straight 24:1,15	77:11,18	355:22 356:8	253:16 256:12
237:21 269:13	178:6	121:20 126:9	356:14,21,23	257:18 267:15
271:19 278:3	Straighten	126:13 141:12	357:8,19,20,23	273:5 282:11
286:21 287:4,4	155:4	141:15,23	358:20,20	283:8 284:4
287:19 291:7	straightforward	142:1,6,11,15	359:12,15	287:3,13
292:15 302:13	63:13	142:19 144:16	360:5,6,7,8,21	296:23 318:16
303:15 305:25	strain 438:15	182:6 212:18	363:5,20,21	321:25 322:18
309:5 318:10	strategies 370:8	215:5 222:5,17	367:20 368:21	322:19 323:15
321:9,19,19	Street 3:7,15	223:18 226:19	368:25 371:10	327:13,13
322:7,19	4:11,20 5:18	233:8 236:13	374:22 376:9	328:8 329:1
323:19 356:22	strength 269:8,8	237:14 238:4	387:4 388:2	332:16 334:1,2
356:23 357:4	269:17 318:9	238:13,24	390:10 391:8	334:3 341:14
357:10 360:8	362:7	239:1,14	392:6,12,14,18	342:14 343:3
456:13	stress 102:19	241:12 244:9	395:1,6 397:16	346:7 349:14
statistician 9:9	444:19	244:19,20	398:20 402:15	356:7 359:12
293:20,21	strike 42:3	245:4,6,18,24	403:15,18,20	359:17 364:9
295:5 296:24	46:17 47:8	246:2,6,15,16	403:20,25	366:2,2 369:3
301:2 307:8,14	63:21 64:22	246:25 247:5	404:8 405:15	370:12,14
308:17,20	72:15 89:15,19	247:16 249:9	407:2 412:2	374:14 381:18
309:4	219:21 275:22	250:19 251:4	415:20 416:5	388:3,22
statisticians	310:6,8,9	252:1,6,6,15	422:21 425:6	389:12,21
301:4,10	stringing 273:7	252:23 253:1,3	428:7 448:14	390:13,23
306:23 307:16	strong 214:25	253:7,9,16	448:22,24	397:22,23
307:17,18	216:22,25	254:5 267:24	452:6 455:14	398:6,6,18,24
statistics 307:10	217:5,11	267:25 268:7,8	456:12 459:23	399:3 402:24
stats 35:13	221:22 222:2	269:11 270:9	459:25 460:3	404:11 405:1
status 309:5	269:10 273:15	285:8 286:4,19	460:10 461:4,5	405:23 406:13

406:17 408:1	468:5,7,9	summary	sure 16:2 20:14	382:22 390:3
409:12 412:22	470:6	167:23 172:9	21:7,24 24:13	400:2,15
413:3,5,8,16	substitute	211:7,13	26:8,10,15	407:15 414:2
413:22 415:17	426:25	272:20 359:14	30:24 32:15	426:11 445:11
416:9,11 417:8	subtlety 136:18	361:4 373:11	39:24 41:19,22	445:11 450:15
423:23 425:12	subtypes 417:14	376:4	44:6,10 46:4	459:8 469:22
428:14,23	success 316:18	summed 286:24	47:17,24 48:2	Surgeon 10:21
429:1 435:22	succinct 70:12	summer 224:11	49:1 53:8,23	364:3 378:4,7
436:2 437:8	such-and-such	super 303:19	63:3 64:21	379:7,24
447:3 448:6	276:25	372:15	65:21 68:20	380:18 393:4
461:20 462:10	suddenly 462:6	superiors	71:14 76:7	surgery 63:6
462:22 463:15	sued 109:8	208:19	79:5 81:10	412:6
studying 102:18	suffered 250:5	supervision	86:19 88:21	surprise 147:7,9
383:5	sufficient 26:24	471:24	91:1 92:3 93:1	198:19
stuff 30:13	59:17 80:4	supplement	93:2 103:20,22	surprised 15:13
70:13 108:12	90:7 125:23	393:4	103:23 108:12	15:17
108:19 181:1	126:6 212:19	supplemental	111:12,14	surveying 407:5
183:18 198:1	379:9 386:9,11	6:21 19:5 20:4	113:18 116:3	407:20
200:15 277:5,6	387:11 396:4	20:6 21:15	117:2 118:5	Susan 7:6 81:9
311:13 319:25	403:25 404:1,2	34:5	122:1 135:7	susceptibility
373:24	404:2,7 457:6	Supplementary	141:8,19	102:22 108:5
sturdy 462:6	457:22	9:12	151:11 155:21	susceptible 47:5
style 102:21	suggest 182:1	supply 110:7	164:16 166:23	suspected
subcommittee	188:14 356:13	support 87:23	167:15 170:5	123:18 125:25
8:6 234:9	469:17,22	89:18,23	170:16 173:3	swamp 93:11
235:23	470:5	194:24 211:16	173:23 175:4	swell 320:8,25
subject 124:17	suggested	234:5 273:6,8	175:10 177:4	sworn 13:23
126:19 127:5	285:11 320:13	312:7 320:8	182:6,17 199:9	471:6 474:14
128:14,17	suggesting	321:1 364:22	201:2 211:14	symptom
472:8	160:25 320:11	415:22 416:5	213:16 226:22	104:21
subjects 282:13	suggestions	421:12 422:22	227:15 230:25	symptoms 7:24
284:3	176:13 177:7	439:7 441:16	243:15 245:19	214:7 371:6
submitted 21:12	suggests 236:18	441:24,25	281:5,10	system 36:8,15
21:21 236:6	271:18 278:2	468:13,17,18	284:24 285:10	104:9,13,14
262:12,15	293:11 444:23	469:5,14	291:23 293:8	250:18
submitting 23:5	Suite 3:8 4:12	supported	295:1,2 296:13	systematic
subscribed	4:20 5:5	418:15	299:8 300:11	10:12 11:13
471:14 474:14	sum 388:9	supportive	301:23 303:8	242:24
subset 286:20	summaries	246:19 418:22	315:18 326:10	
substance	165:9,20,23	436:21,21	331:8 333:6	T
173:20 174:4	167:1 168:2,9	445:21 463:4	347:24 349:1	T 5:16 6:1,1,8
174:15 176:18	168:16 170:6	supports 37:3	350:8,17	7:1 8:1 9:1
184:2 474:7	summarize	273:3 384:6	351:21 355:2,8	10:1 11:1 12:1
substances	165:6 309:9	419:25 420:22	355:18 358:10	473:2
448:21	343:12 356:11	423:8	361:5 364:24	T-A-H-E-R
substantive	Summarizing	supposed 385:3	373:12 375:9	424:2
183:13 184:10	236:10,12	454:15	375:11 377:4	table 11:4 171:5

171:5 250:8,10 328:9,25 330:10 334:21 336:8,9 340:24 350:23,25 351:2 394:5 396:20,21 397:14 399:14 tables 257:14 Taher 266:25 271:17 278:1 359:12,17 423:22,23 424:5,12 take 23:9 41:13 42:20 44:11 56:15 82:17 92:20 99:11 103:19 136:5 139:8 153:3 154:12 183:25 190:4 203:22 204:2,12,15 209:25 213:13 216:18 255:8 257:18 263:8 263:15 268:18 282:24 298:9 299:25 300:6 300:16 308:11 320:15,17 329:13 340:5 340:17 343:15 353:21 365:7 369:15 377:8 386:18 387:15 388:2,3 416:16 426:9 430:22 431:22 434:20 439:17 440:1,1 440:3 446:17 454:21 taken 14:13 15:11 19:17 81:21,22 197:23 471:4 takes 383:20	talc 8:11 9:21 11:12,18 55:3 75:25 76:13,16 76:21,25 78:21 126:19 127:5 134:10 211:19 215:4,6 222:5 223:17 225:22 240:16 259:10 259:11,15,16 259:17,18,23 259:25 261:14 270:10 271:21 273:1 278:5 280:25 281:3 285:13,15,19 286:2 329:1 331:2 339:22 345:1 359:3 384:20 399:22 400:13,16 401:4,8,20,21 401:23 412:8 412:11,16,23 416:6 417:11 417:14,17 418:16,17 422:12 423:19 424:14 427:12 428:6,8,20 429:6,19 432:3 432:10 433:6 434:1 435:23 436:25 437:9 439:9,12 448:8 448:16,16,19 449:2 452:15 452:18 453:19 talc's 422:10 Talc/Ovarian 9:16 talcs 285:24 286:9 talcum 1:5 13:11 28:14,19 49:3 50:7,13 59:3,11 60:2	63:23 64:5,24 69:11 72:6,18 74:23 75:4 76:2 77:12,14 77:14 78:3,10 78:17 79:17 80:9,13 84:11 84:16,21 89:15 89:17,19,21,23 109:21 111:2,7 111:9 120:20 126:9,14,19 127:11 128:17 129:3,13,25 130:25 131:15 132:7 134:15 134:19 135:5 135:14 136:7 136:20 137:2 137:20 138:8 140:22 142:12 142:16 148:16 149:21 150:20 151:4 163:3,7 163:13,18 164:12 165:24 167:2,12 187:6 199:1,12,25 200:3,10,22 201:3,9,23 202:21 203:1 209:18 210:23 211:17 212:21 214:19,23 216:20 217:9 218:2 219:7 220:11 221:5 231:16 233:23 234:10,12,21 236:14 237:15 240:17 241:7 241:10 261:14 262:7 263:15 263:16 264:1,2 266:17 272:15 273:22 274:14 275:1 276:1	278:22 279:1 280:23 329:6 368:17 382:12 384:5,7,18 385:21,23 406:14 407:7 410:22 411:5 411:10,22 415:8,15,21,23 435:17 436:13 451:24 453:5 460:10,11,25 462:19 464:3 talk 24:24 31:5 31:6 34:1 40:10 44:2 46:8,9 59:15 59:20 71:12 80:19 86:20 99:9 121:1 125:6,12 151:22 156:22 163:6 177:21 184:14,16,24 184:25 211:22 216:2 219:16 238:7 239:21 243:3,5 250:25 297:13 314:19 315:18 319:15 337:13 360:19 361:8 374:20 376:21 399:20 444:11 447:2 454:25 459:14 461:22 463:7 talk- 28:17 talked 141:9 153:5 162:16 203:15 335:23 355:21,25 428:15 435:15 435:16,23 436:4,4 452:4 457:18 talking 28:12 40:24 47:25	58:1,11,22 69:25 72:21 73:25 74:1,4 79:25 80:6 81:3 90:4,9 99:21 111:1 117:15,17 118:7,19 135:9 136:24 163:9 167:7,9,10,15 167:16 170:7 170:19 174:16 192:13 195:8 197:19 199:25 201:3 223:2,11 241:6 244:17 245:3 246:14 247:4 262:20 263:10 276:23 280:20 299:8 303:7,11 315:1 317:22 321:3 323:4 337:14 375:23 384:23 386:10 387:5 387:23 390:7 393:7 402:5 403:21 406:8 408:10 409:23 412:4 419:7 421:25 447:24 449:12 452:5 454:5,7,8,9 455:24 456:2 459:10,13 461:13 465:14 466:7,10,14,18 talks 92:2 214:13 278:14 418:10 task 190:4 462:8 tasks 178:18 Taylor 8:22 team 175:18,25 teaming 132:24 tear 29:22 343:5 technical 196:20
---	---	--	---	--

269:6	90:9 144:8	355:23 356:11	thereof 304:1,23	463:12 468:24
Tecum 6:13,18	224:22 225:9	356:12 407:21	471:11,14	think 14:16 17:9
tell 26:21 50:17	240:1,8,20	412:15 415:9	thing 32:9 85:11	18:8 20:24
51:24 69:9	245:6 260:13	429:15 432:6	86:16 111:24	24:18 25:20
73:11 79:9	335:1 337:7	436:18 449:7	118:7 164:15	28:21 29:15
122:12 141:8	347:25 363:11	453:8 471:7	205:24 212:12	30:16,20 40:3
143:9 157:11	452:5 456:24	testing 64:4,19	215:1,2 248:14	41:19 42:25
157:15 162:4	terrible 461:25	69:10 70:8	277:3 287:18	43:21 46:3
179:1 183:16	462:1	74:12,22	299:7 309:6	48:8 49:13
186:2 192:24	Terry 238:1	120:10,14,16	313:20 324:8	53:16 56:9
218:17 219:9	463:18,18	120:20 291:10	408:11 425:3	57:25 65:2
245:23 248:5	test 37:9 70:18	292:21 302:5	445:8 447:4	67:4,6,8,18
248:11 249:8	71:18 207:22	315:11 316:11	456:1 469:10	68:12,13 70:15
249:14,21	424:21	tests 64:17 72:17	things 20:16	71:20 73:11,24
250:4,17	tested 63:23	text 265:11	21:3,19 52:17	74:4,18 75:21
273:14 277:11	64:24 72:7	331:10	59:15 61:11	77:9 79:5,7,23
283:15 320:15	testified 13:24	thank 19:19,20	64:18 69:1	85:18 88:12
334:4 341:24	159:16,17	19:25 35:18	73:2 92:3 97:7	90:10,17,20,21
342:3 344:18	177:16 206:24	39:2 44:24	104:19 116:8	90:22,24 93:22
387:23 389:10	207:9 233:19	45:5 54:8 58:6	117:3 125:22	97:6 106:9,12
390:2 391:7	234:8,11	63:2 74:10	130:19 142:2,3	106:23 107:25
405:17 468:16	384:14 428:16	76:23 80:23	143:11,16	109:19 112:20
469:6	431:21 432:1	87:8,22 88:25	144:16 146:18	113:5 116:9,20
telling 160:13	testify 137:1	89:13 100:5,11	158:3,6 162:11	117:2 118:2,16
460:15,18	138:3 160:11	101:18 119:5	162:12 168:22	120:13 121:17
tells 434:8	466:18	127:1 139:5,9	168:25 169:3	124:25,25
temporality	testifying	147:1,2 188:12	170:6 171:3	126:21 130:7,8
269:19 270:19	160:24 206:3	210:2 215:11	175:15 176:10	131:16,21
270:19	testimony 7:20	227:4,9 252:4	178:16 183:24	133:13 135:12
ten 33:5 130:5	20:23 32:2	272:4 282:7	202:11 203:19	136:20 137:23
137:13 152:14	43:19,22 67:12	283:23 287:10	215:19 223:9	138:10 139:6
152:19,20	67:16 88:7	325:2,21 327:7	224:15 239:3	139:19 140:8
155:14,20,24	109:17 129:19	327:7 330:17	239:12 253:24	142:7,9 143:11
185:15 189:18	132:13 137:25	338:18 349:6	256:21 257:10	143:21 150:23
331:10 333:5	138:12 139:18	364:18 377:20	263:1 266:9,20	152:7 153:2,9
340:18 341:2	139:24,25	381:13 397:8	269:12 273:7	154:18 161:3,9
343:23 344:14	150:22 151:7	400:10,10,11	291:16 308:13	162:7,8,10,17
tend 70:7	153:18 163:2	419:17 431:3	308:14 310:22	162:18,23
tens 155:24	163:15 171:12	431:20 437:13	311:3 332:6	163:1,8 164:14
408:1	172:12 176:3	443:7 470:12	334:24 340:24	165:8 166:21
term 196:20	191:15 205:25	470:13,14	357:23 375:2	167:22 170:17
269:6 447:1,6	206:8 232:1	thanks 14:3	385:2 386:5	182:23 184:12
450:25 459:7	233:20 237:3	82:15 166:11	404:3 412:7,9	185:21 189:22
terminology	259:4 264:5	301:9 470:10	412:10 415:2	191:23 195:8
73:10 130:6	279:9,14 315:6	theory 76:14	426:15 442:4	197:8,25
terms 20:24	323:22 336:22	201:13,17	452:4,13	198:11 199:23
70:12 73:21	345:4,15	420:23 439:8	459:15 462:12	201:21 202:11

205:24 206:21 210:13 211:23 217:1,3,16 218:18,25 219:18 220:7,8 221:12 223:8 223:10 224:5 226:6,8 229:18 229:25 230:16 230:17,18 237:1,3,23 238:4 240:18 243:2 244:12 245:22 246:14 252:17 253:13 253:18 254:20 255:3,5 257:25 258:8 260:1 264:15,17 270:24 272:18 273:8 276:22 276:23 278:18 278:21 279:11 279:15,18,19 280:20,22 281:9 283:7,15 287:12,15,17 293:4,14,17,17 294:16 296:9 297:11 301:20 301:21 303:10 303:12 305:1,2 306:9,9,13,15 306:19 311:11 311:12 315:20 319:16 321:24 321:25 322:10 322:13 323:3 323:14 325:19 330:7 331:6 332:17 334:8 337:1,7 340:12 340:17 342:20 343:8,19,20,22 345:12 352:12 353:16,20 355:24 356:9	358:8,11,18,22 358:23,23 361:9,12,19 362:1,11,12 364:3 371:9 372:17 374:1 374:13 375:23 380:13 386:24 387:1 388:1,8 388:16 389:21 389:22 390:6 390:22 392:2 392:10,11,13 392:18 394:11 401:19,23,24 410:10 412:3 418:14 421:11 425:11 430:15 432:6 435:9 436:1,19 447:21 451:7 451:11,12,13 452:10 456:2,9 456:10 458:15 460:24 463:14 464:10 466:7 469:1,3 thinking 40:1 48:16 49:10 70:1 144:7 392:21 thinks 361:20 434:9 third 8:20 48:3 64:10 101:7 236:8 290:2,14 290:18 369:22 389:21 432:22 third-party 176:20 thirty 472:12 THOMAS 3:13 5:16 thoroughly 322:1 thought 66:19 69:25 72:22	116:12,16 190:10 206:2 227:9,11,16 238:24 241:6 251:22 254:6 257:18 291:16 294:22 307:15 307:17 316:22 366:8,10 461:21 thought-prov... 301:9 thoughts 126:2 233:10 thousands 408:1 three 22:18 23:7 43:14 57:14 183:12 245:7,8 245:8,9 267:15 290:6 297:13 318:3 331:11 349:20 350:6,7 390:11 430:16 432:22 459:25 459:25 threshold 302:14 305:21 318:19 319:9 319:13 362:9 362:12 threw 440:14 throw 29:23 Tiernan 8:5 tight 44:3 Tim 289:12 290:14 time 13:6 19:10 19:13 21:1 23:1 27:13,15 27:19 42:20 44:15,18 46:13 49:12 55:24 57:11 71:12 83:3 88:20,22 89:3,6 91:2,13 114:8 117:16 128:8 151:10	151:16,19 152:2 153:2 163:17 173:15 175:17,25 176:5 177:13 177:13 178:1,7 183:23,24 185:6,12 187:17 189:25 197:24 202:19 204:5,19,22 218:22 227:22 229:25 241:15 257:24 258:9 258:21 265:13 270:20,21 280:6,10,13 282:24 299:14 301:17 314:16 315:19 320:18 320:21 338:13 338:16 349:4 349:22 374:5 376:22 377:9 377:12 381:10 387:9 426:14 426:16,19 447:10,13 464:12,15,19 464:22 470:11 470:16 471:5,6 471:8 timeline 29:9 times 14:13 28:8 57:15,24 117:21 155:17 189:6 259:3 389:6 453:23 Timothy 289:6 289:12 tiny 361:16 371:14 TISI 3:12 100:9 132:21,24 289:21 431:8 tissue 282:14 284:10	title 297:5 389:17,18 Tobacco 10:20 378:7 today 13:16,20 15:2,13 19:22 19:24 22:22 27:9 34:6,7 43:19 53:7 68:5 69:9 71:16 75:5 111:17 121:14 130:22 145:3 157:25 160:11 161:4 205:14 205:23 257:21 298:7 300:21 318:9 329:24 338:23 340:5 363:10 367:25 412:14 427:2 433:19 435:15 462:16 467:25 468:12 469:4 Today's 13:6 Todd 1:25 2:16 13:20 471:18 toe 107:11 told 15:14 115:6 162:11 221:1 244:16 430:9 454:18 tolerance 84:10 Tom 325:19 348:23 430:13 430:18,18,18 430:18 431:9 ton 373:23 tone 106:7,9 113:14,19 115:2 tools 238:23 top 66:7 84:1 93:9 95:23 161:15 197:10 243:8 284:16 284:18 328:8
--	---	--	--	---

396:21 414:20 topic 48:15 77:10 123:22 124:13 128:25 129:3,12 131:12,24 134:15 140:21 144:13 150:3 151:4 156:3 163:23 164:11 189:9 199:14 200:3 203:1 223:3,11 232:6 240:7 245:10 303:12 313:18 315:18 408:25 448:15 453:17 topics 141:25 143:13,14,15 162:25 254:15 260:2 tore 30:3 total 179:23 388:9 420:25 462:20 463:3 totality 383:21 384:3 totally 204:18 touched 69:5 touching 332:5 tough 332:17 Towson 1:16 2:7 13:10 15:2 Toxicological 262:3,5 toxicologist 119:17 Toxicology 262:9 toxin 450:21 toxins 120:11 Trabert 22:9 track 327:10 traction 315:15 traffic-related 376:2 trailed 348:25	trained 52:15 training 117:5,6 230:1 transcribed 471:10 transcript 6:9 7:2 8:2 9:2 10:2 11:2 12:2 22:13 86:3 471:10,12,21 472:13,14 transcription 474:4 transcripts 60:8 167:24 231:21 Translational 9:8 294:14 308:16 309:21 310:12 transport 273:3 284:19 285:6 transvaginal 284:21 285:7 413:11 traveled 230:12 treat 60:14 62:1 62:1 treatment 61:6 63:12 115:23 116:6,25 118:9 treats 61:1 trending 352:8 trial 128:10 138:3 188:14 trials 128:4,6,12 128:16 246:21 trick 133:7 tricky 41:18 tried 238:12,18 238:24 239:2 240:13 245:17 245:19 246:1 246:16 247:8 251:7 333:14 338:25 358:22 359:1 447:22 461:19	tripping 184:24 trouble 87:5 true 41:24 90:22 90:24 103:15 108:7 121:13 218:4,25 226:6 226:6 257:24 294:25 303:3,9 314:7 381:10 383:24 384:4 388:11 418:21 418:23 436:2 437:7 455:11 458:19 465:25 466:21 471:10 Trust 219:17 truth 37:2 331:22,25 463:5 469:19 469:24 470:7 truthful 14:23 434:19 truthfully 73:19 160:11 274:18 try 32:19 38:5 48:3 55:20 111:25 115:10 133:6 149:11 179:21 183:24 198:12,14 216:15 266:16 310:22 352:23 408:10 463:7 trying 48:8 53:6 73:3 106:10,12 118:13 122:3 130:14 131:21 133:7 135:6 156:16 167:15 168:6,12 170:24 172:18 177:19,19 179:20 184:6 184:24 189:19 190:3 191:13 194:13 198:12 200:24 202:19	246:2 251:14 257:11 266:15 266:20 278:18 284:25 288:16 294:16 296:8 311:21 331:6 337:1 338:20 340:14 342:11 343:7,9,11 352:12,13 360:2 361:10 376:23 385:2 386:22 453:12 453:14 462:9 469:1 tubal 285:16 tubes 417:18 TUESDAY 1:17 turn 52:21 193:24 210:24 212:1,2 214:16 244:14 256:5 305:5 324:2 394:6 423:20 turned 227:2 turns 104:21 twice 245:15 345:13,18 two 22:18 43:15 73:2 92:25 101:3 112:21 121:24 131:4 139:7 183:11 196:25 217:17 218:25 243:7,8 256:11 258:9 285:24 305:24 306:10 308:14 312:3 313:10 314:3 321:12 323:9,18 346:11,13 349:14,20 350:6,7 351:12 351:14 354:24 354:25 360:15 388:16,17	389:22,23 432:22 441:20 two-minute 176:6 two-sided 140:8 type 56:7 64:8 102:1 134:25 158:6 165:24 167:1 180:18 188:2 250:4 269:16 358:4 360:24 368:3 392:18 458:5,6 458:8 469:14 typed 20:20 types 103:17 180:11 267:15 359:11 368:1 401:3 404:18 typical 387:7 465:16 typically 266:6 typing 20:9 91:15 typo 94:8 typos 168:24 176:9 181:17 469:7 Tzonou 351:23 352:15 <hr/> U <hr/> Uh 328:21 ultimately 239:8 Ultrastructural 11:15 427:9 Um 344:24 379:25 uncertain 417:16 418:3 uncertainty 301:8 455:1,4 455:5 unclear 28:22 62:14,16 283:18 284:6 286:4
---	--	--	---	--

uncontroverted 233:20	422:15 428:22 428:25 440:16	university 15:6 93:19 100:19	309:5,12,24,25 311:1 316:16	342:5 461:14
underbelly 360:3	448:12 450:12 453:14 460:20	153:12 208:10 223:14 224:17	316:19 317:9 317:10 329:1,5	validated 460:25
undergraduate 94:23	understanding 17:24 39:15	314:9 320:3 unprecedented 462:2	330:11 331:2 331:13 332:24	validity 239:22
underlying 326:13 392:13	40:13,18 51:14 52:14 59:22	unpublished 359:22	334:18 339:22 340:8 343:25	Valley 2:6 13:10
443:11	64:3 72:4,10 109:2,14,24	unravel 245:16	344:14,25 345:1 346:21	value 341:1
Underneath 350:19	110:3,10 130:24 158:9	unreliable 331:17 340:19	361:2,18 362:13 368:12	variables 249:22
underpinning 72:2	166:19 170:25 176:21 178:9	update 242:6 updated 213:18	392:2 404:9,18 413:9 414:17	variety 203:18
underpinnings 205:20 254:2	180:11 363:23 405:5	updating 92:4 92:23	417:11,15 421:17 428:6	359:4 363:4
underpowered 342:17	understandings 33:3	upper 285:1 upside 449:14	446:25 useful 29:23	404:9,24
undersigned 471:2	understands 80:21 330:7	463:1,17 urgency 315:8	239:9 users 280:23	various 165:15
understand 14:6 14:12,17,20,22	understood 61:12 70:15	315:22 urgent 93:8	281:1 331:10 365:5,17	171:12 242:25
24:5 29:13	80:22 144:5 156:22 203:6	urging 295:20 309:23	428:20 USGS 400:25	341:17 455:14
32:10,13 37:9	381:10 undertaken 394:2	urine 404:25 405:25	usual 14:4,11 449:14	vast 245:19
41:17 60:12,15	underway 286:5 underwear 331:14	usage 50:20 use 9:21 11:9,12	uterine 417:18 uterus 254:9	Venter 285:9
64:12 67:11,23	unexposed 366:21 428:16	46:12 51:17 54:21 59:10	412:7 utilize 186:23	verbally 244:16
73:9,25 81:25	428:16 unfortunately 237:4	71:9 75:6 76:16,21,25	<hr/> V <hr/> V 3:12	verify 20:16
82:3,4 103:21	uniformly 461:4 uninformative 343:24	78:18 80:14 84:23 93:4	vagina 411:11 411:23 412:7	version 213:17
109:20 121:8	unique 247:14 unit 104:10	119:23 149:4 154:19 168:1	416:7 417:17 418:6 433:8	versus 318:10
124:24 133:9	105:13,23,24 105:25 106:1	195:23 198:15 211:17 214:23	435:2 449:16 vaginal 285:11	348:8 356:8
135:7 144:4	United 1:1 13:14 36:22 367:14	216:20 217:9 218:2 219:7,22	430:3 vaginas 254:9	357:19 366:20
154:11 162:2	434:12 universe 251:14	220:11 221:5 233:23 240:13	254:12 vague 111:23	vertical 353:18
167:14 177:20	293:12	242:18 263:12 264:2 272:15	149:24 220:5 230:11 231:4	vice 294:6
179:21 180:8		273:21 274:14 290:24 291:9	Valentin 9:13 valid 239:15	video 13:7,8
180:10 191:14		292:20 307:10		videographer 5:23 13:3,5
207:6,17				14:7 19:10,13
232:24 233:5				19:23 44:15,18
251:14 253:21				44:23 89:3,6
253:24 254:1				89:10 151:16
254:10 255:9				151:19 204:19
256:22 257:17				204:22 280:10
266:8 318:8				280:13 320:18
326:21 352:12				320:21 338:13
354:20 375:5				338:16 376:25
382:17,20,21				377:9,12,22
385:20 389:16				426:16,19
400:15 408:8				447:10,13
410:24 411:3				464:12,15,19
				464:22 467:13
				470:16
				videotaped 1:14
				6:11,16 17:16
				470:18
				view 171:8
				225:10 246:19
				306:19,20

violates 160:19	65:20 73:14	346:21	146:18 165:4	347:14 351:19
violating 337:24	86:22 93:2,11	wanting 172:24	172:17 183:22	365:9 393:4
violative 160:21	93:16 96:15	wants 223:15	190:5 196:21	396:24 400:19
virtually 198:19	99:5,6 103:19	439:16,24	198:14 201:8	404:9 406:10
virtue 395:21	114:25 122:14	444:10	207:19 211:23	416:17 437:12
vitae 7:9 91:3,11	140:11 151:22	War 226:19	215:4 217:16	444:13
91:24 92:10	152:16 159:4	392:22	219:1 222:5	we're 14:9 19:11
127:10,19	160:5 161:15	warmer 44:8	223:18 229:15	19:14,16 27:8
146:10 364:21	162:2,4 168:8	warning 51:16	230:11 238:19	28:12 32:18
390:10	175:24 176:7	51:24 54:18	244:11 258:8	33:15 34:1
vitro 252:1,6,14	180:8,10	57:2,22 58:1	263:12 275:8	37:23 44:1,16
252:15,23	183:17,19,20	58:12 75:6	283:13 301:11	44:23 47:24
253:15	183:21,22	295:19	342:25 371:2	58:1,5,22
vivo 252:14	189:8 203:20	warnings 51:22	375:24 377:14	72:21 73:25
253:1,15	203:21,22,25	56:22	382:5 401:17	74:1 77:24
vocabulary	204:2,10,11,12	Washington 3:9	404:22 405:21	81:3,18 82:8
447:2	204:15 217:19	4:13 5:12,19	415:4,16	85:5 86:20
voice 81:24	241:23 251:18	wasn't 29:23	429:13 447:1	89:4,7 105:18
115:7,8	252:12 254:1	47:15 50:15	454:14 456:9	113:5,21 114:2
void 471:13	276:18 279:13	61:14 139:19	456:10 465:19	118:7 130:21
volume 10:24	293:3 316:7,18	156:25 179:23	467:24	136:24 151:17
195:21 296:24	317:3,7 319:2	188:15 216:12	ways 46:11	156:16 163:9
405:20	319:7,8,14	231:6,6 246:2	115:11 219:19	167:7,9,9,15
vote 455:15,25	320:16 326:7	246:19 250:20	223:23 224:5	167:16 170:7,9
vulnerable	326:17 331:22	250:23 252:21	285:23 314:13	172:14 183:18
370:7	331:23,24	253:23 283:11	317:1 403:19	197:19 199:23
	332:2 337:6	320:1 323:10	445:21	201:14 204:23
W	338:6 341:11	342:10,10	we'll 14:10 19:2	209:10 213:23
wait 61:18 62:21	341:12 343:24	343:4,5,9	19:18 25:23	216:3 223:11
68:23,23,23	344:11 351:6	345:10 389:25	29:9 40:10	229:4 245:3
144:1 200:13	353:4,20	391:10 425:1	52:9 59:20	246:14 247:4
210:17 234:17	358:12,25	462:8,9	83:12 91:3	263:10 280:14
234:17 247:7	363:17 372:15	Wasserstein	95:8 98:22	280:20 289:21
258:14 270:2	374:4 377:3	298:6 309:7,22	132:17 138:14	294:11 299:7
274:22 275:13	379:6 384:12	310:15 320:12	138:17,21	304:13 311:14
276:13,13	394:6 399:24	Wassertine	139:8 151:15	311:15 317:22
293:2 303:1,1	413:25 424:16	310:15	152:2,12 211:1	320:19,22
318:2 335:5	425:9 430:21	waste 27:13,15	212:8 213:3,7	323:3 338:5,14
346:4 358:8	432:15 438:15	218:21 306:1	235:16 238:7	338:17 342:20
361:25 377:6	438:18 440:19	watered 221:12	250:25 267:7	350:2 359:11
444:12 466:11	449:21 465:13	way 17:9 39:9	271:11 275:11	365:10 372:16
467:14	wanted 29:21	40:5 41:19	291:19 297:13	376:22 377:10
walk 218:20	30:2 32:25	46:4 59:15,16	299:19 311:23	377:13,14
want 18:17	40:1 99:16,25	69:7 71:20	312:4 315:15	387:21,23
20:14 24:6,24	190:2 194:23	73:3 74:6	320:17 326:14	408:10 412:4
27:14 32:15,22	251:20 253:20	75:12 105:18	328:14 337:16	419:7 426:17
42:9 62:9	275:19 313:21	107:24 108:19	338:6,11,11	426:20,24

447:11,14,24	well-respected	18:8 20:24	141:1,14,20	224:4 225:4
449:12 452:5	260:4	21:18 22:8	143:7,21 144:6	226:3 228:9,14
454:8,9 455:24	went 93:10	23:21,23 24:18	144:21 145:9	229:24 230:21
459:10 463:6	150:24 203:23	29:3 31:8	145:18 146:15	231:5,20 232:8
464:13,16,20	233:20 316:22	32:21 35:9	147:1,9,19,25	232:19 233:5
464:23 465:14	333:8 338:22	36:1,25 39:21	148:19 149:2	233:16 235:9
466:7	weren't 50:15	40:17 41:18	149:16,25	237:1 244:3
we've 57:23	230:9 241:15	42:22 43:5,21	150:23 151:8	246:1,11
58:11 85:4	246:22 293:16	47:11,14,24	151:12 152:12	247:25 248:8
157:17 226:4	307:5 379:5,5	48:13 49:7,23	153:19 155:2	248:18,25
316:19 317:10	425:3 456:13	51:1,10,20	156:13,23	249:12,18,25
317:10 329:24	Western 102:21	55:2,17,19	157:11 159:14	250:7,23 251:7
349:8 358:11	108:4	56:3,9,21	159:24 160:8	255:3,16
359:18,22	Western-style	57:16,25 58:15	167:7 168:21	256:19 258:24
368:16 402:5	102:22	59:6,13 60:5	169:14,21	259:12 260:11
404:19,22,24	whatsoever	60:19 61:5	170:16 171:17	261:3,18,25
427:1 433:18	383:19	62:5,15 63:25	172:14 173:23	262:20,25
435:23 436:17	wheelhouse	64:8 65:2,13	174:7,12 175:6	263:21 264:6
449:10 468:6	254:25	69:15,21 72:10	175:13 176:4	265:4,22 266:2
weak 269:10	WHI 232:25	72:20 73:9,17	178:14 179:1,9	267:20 268:3
360:21,22,25	233:14,16	73:20 74:18	180:7 181:1,10	268:13,20
361:5,22 362:3	whisper 226:25	75:1,9,12,18	182:19 183:2,8	272:18 274:3,5
362:22 363:11	Whitnum	79:1,4,23 82:3	184:20 187:14	274:20 275:7
weaknesses	388:21 391:8	85:7,10 86:15	187:22 188:7	275:16 276:17
460:10	457:12	86:20 87:3	188:10,13	278:13 279:10
web-based	Whittemore	88:8,19,23,25	189:3,23	279:15 281:9
238:23	285:11 351:15	90:3,16 96:19	190:23 191:22	281:16 282:22
website 7:12	whoa 99:10	97:23 98:9	192:6,11	282:25 286:11
95:9 96:3 98:5	160:9,9,9	99:1,12 103:19	193:21 194:2	287:11 288:2
100:8 101:20	440:23,23	104:3 105:11	194:12 195:7	288:10 289:3,9
101:25 188:2	widely 49:4,14	106:8,23 107:5	195:19 196:11	289:14 291:15
223:15 224:9	widespread	107:18 108:24	197:14,18	293:2 299:4,13
224:11 225:15	295:15	109:5,19 110:2	198:8,22 199:4	300:7,17
316:23	wielding 253:22	110:17 111:12	200:10 201:16	301:20 302:19
websites 213:20	wife 229:3,8	111:24 116:1	202:2,10 203:9	303:2 304:7
224:15	Wignall 398:5	116:16 117:12	204:7,13,17	305:1 306:8
wedded 323:5	wildly 161:1,5	118:2,13 119:1	205:11,18	307:3,8 310:21
week 17:6 93:14	William 66:10	120:18 124:1	206:11,20,25	314:11 315:7
133:1 313:12	66:16,24	124:25 125:9	207:1,19	318:14 321:12
weighing 321:17	wish 274:10	125:15 127:15	208:21 209:4	321:23 322:10
weight 321:8	299:13 319:4	127:23 128:22	209:11,21	322:22 323:23
WEIL 4:19	330:20 334:5	129:20 130:5	210:13 215:18	331:5,19
weird 394:12	340:5	130:18 131:6	216:11 218:9	333:20 334:11
Weiss 348:3,7	withdraw 61:20	131:12,18	218:11,24	334:21 336:4
welcome 89:2	62:19	134:22 135:25	219:12,18	336:24 339:5
343:25	witness 2:19	137:12,23	220:19 221:21	339:18 340:12
well- 260:8	15:19 16:7	139:7 140:8	222:10 223:2,8	342:19 343:19

345:23 347:15	443:23 444:8	69:7 71:9 97:9	191:3,3,7	296:25 308:18
348:7 349:13	445:5,19 446:6	123:12,23	192:1,2 193:11	309:3,22 315:9
350:24 351:6	446:24 447:20	124:10,12	194:23,25	315:10,24
352:4,11	448:13 449:9	125:2 147:4	195:21 198:13	316:2,3,4,5,6,7
354:17 356:5	450:11,24	168:22 169:17	199:6 200:5	317:7 318:19
357:1,14	451:11 452:3	169:18 170:13	225:6 230:6	392:21 456:1
358:11 360:14	452:21 453:9	170:14 187:22	231:7,9 256:25	world-renown...
361:25 362:11	455:8,17,24	240:24 241:1	339:5 367:7,10	260:23
363:1,14 364:3	456:19 457:2,9	241:17 268:24	378:11 407:5	worried 362:18
367:19 368:8	457:25 458:22	269:3,4,5	407:19 408:14	worries 177:4
368:20 371:20	460:20,23	270:15 272:3	408:22 409:4	291:23 366:9
372:6,15 373:4	461:11 463:21	273:16 293:10	450:25 452:13	worsening
373:18,23	464:10 466:5	303:13 313:6	467:3	372:19 376:12
375:9,11,15,22	466:13 467:1	333:21 361:2	work-product	worth 16:8
376:17,22	467:15 470:2,9	378:9 405:6	33:10 161:25	197:24 257:11
377:2,5 380:5	470:14 471:6,7	442:9 460:6	166:13 177:10	wouldn't 15:13
380:13 381:9	471:14 472:1	468:5	worked 23:16	21:18 36:17
381:21 382:4	Wolfson 71:5	worded 221:17	56:5 69:8	40:7 48:22
382:17 383:8	219:4 220:9,15	words 70:9	152:24 174:24	51:22,23 56:23
384:11 385:1,7	woman 63:17	91:15 119:23	182:5,5 185:18	56:23 57:6,7
385:10,17	115:23 116:6	147:7 149:4	186:3,9,15,22	63:4 71:9 72:1
386:1 389:10	116:25 117:19	167:14 169:23	190:5 192:6	106:14 116:23
390:4,22 391:6	118:9 119:7	170:4,17,20	195:20 229:13	147:9 149:16
391:20 392:1	152:24 175:9	194:14 240:13	230:10 388:4	149:17 197:23
393:6,11	woman's 412:17	240:18 270:23	402:14	197:23 207:21
394:13 396:9	women 34:25	320:14 360:24	worked-out	215:18 231:5
396:16 399:24	35:6 36:21	360:25 361:1	281:17	311:5 323:11
400:15 401:17	59:2 60:14	work 33:8,12,15	worker 392:17	323:11 340:24
402:12,19	61:1 62:1,3	37:25 38:12	working 176:23	342:3 368:11
405:13 408:24	215:9 226:13	48:17 56:1	183:18 185:1	382:4 383:18
409:15 410:7,9	234:12 236:14	63:6 92:20	185:14 187:5	409:23 410:14
411:3,15,19	236:18 237:15	104:10 128:20	202:21 261:10	449:17 452:19
412:2,22	250:5 280:22	128:25 129:2,6	261:13 387:9	452:21
413:16 415:1	282:15 283:18	129:6 130:20	394:9,20,22	Wow 446:6
416:14 418:1	284:6 285:15	135:8,17 136:6	395:10 396:1	write 145:19
418:21 419:7	286:3,3 331:16	152:14 154:20	398:20 402:5,6	149:5,9 154:23
420:20 421:7	340:18 387:8,8	156:24 157:9	works 81:25	168:18,21
421:15 422:17	388:3,22 391:8	158:13 159:20	105:19 129:6	206:16 219:20
423:12,25	395:1 410:18	160:2 163:18	153:13 313:8	240:3 243:2
426:11,14	412:5 428:17	163:22,24	319:18 320:3	311:2 316:7
428:19 429:3	428:19,24	173:19 175:2	world 8:23 9:10	409:9 437:7
429:16,22	449:13	176:16 178:23	57:17 80:1	468:4
430:10,16	wonderful 114:6	179:6,13 180:5	81:4 90:19	writers 436:25
432:17 433:14	wondering	181:5 185:22	98:6 135:6	writing 30:21
434:5,22 435:8	204:3,8 301:3	185:25 186:17	226:19 260:18	33:19 233:7
435:20 436:19	Wong 350:20,22	187:12 189:13	265:18 268:22	395:24 468:1
437:5,23 442:4	word 46:12 53:7	189:16 190:16	270:16,20	writings 33:2

170:3 356:13 written 130:20 130:25 134:25 145:9 309:7 322:11 409:24 453:18 456:3 wrong 53:14 56:21 76:20 116:9 130:6 153:10 222:13 258:1 270:15 318:2 348:3,5 348:15 wrote 181:21 206:18 257:9 355:25 435:9 470:6 Wu 351:13,14	170:2 171:14 174:12 175:6 178:5 179:10 179:25 180:14 181:14 182:19 194:2 195:17 195:17 199:21 200:19 204:7,9 207:8 209:8,8 209:8 216:8,23 220:21 221:11 227:9,19,22 229:7 242:8 243:13 245:5 252:4,10,17 254:13 257:13 259:16 264:7 265:14 269:6 275:7 280:8 282:25 291:22 296:12,16 299:17 300:16 304:9 307:21 310:9 311:25 313:2 314:3,7 316:2,5 317:18 317:25 320:14 325:20 328:1 330:14,18 331:19 338:8 342:15 350:5 351:5 356:5 359:21 365:8 365:21 366:17 367:5,12 370:13 378:13 386:20 388:18 398:7,8,9 399:19 400:6 403:7 417:8 419:11,18 420:19 426:14 436:6 438:6 446:9 454:12 456:2 year 36:21 49:20 389:11,17	years 33:5 45:21 46:2 51:2 108:17 152:14 152:19,20 155:14 175:1 185:15 189:18 201:23 316:20 391:9 418:4,9 445:6,7,9 457:13 458:10 458:17,18 yell 113:12 218:12 yelling 115:4 218:16 219:12 219:14,16 yellow 30:18,22 yep 204:18 211:14 212:12 212:15 215:3 285:4 328:23 367:5 417:2,4 yes/no 371:13 404:6 yesterday 17:12 yielded 331:16 yields 340:19 York 5:11	0 0.01 319:12 0.03 351:1 0.05 8:23 297:1 302:14 305:22 308:18 309:23 311:15 316:16 316:17 318:20 319:1,11 351:1 361:8 0.05' 9:11 0.40 328:19 0.5 319:4 0.7 328:18 329:6 329:7 330:12 336:14 339:23 340:25 343:15 344:15,23 0.70 330:20 332:15 333:17 334:8 347:5 0.8 367:17 0.94 359:25 000004999 8:18 000005003 8:18 000013131 9:22 07701 3:22 08542-3792 4:21	1.01 352:21 361:15 1.02 352:21 1.03 352:21 1.05 352:16 353:3 1.1 353:20 367:17 368:3 368:15 400:21 1.10 328:19 1.16 365:23 1.163 365:14 1.17 399:11 1.18 367:1 1.2 353:10,20,21 354:3,10,12,13 354:14,15,20 354:22,23 355:4,9 361:19 365:6 367:17 368:4,15 379:16,23 1.23 367:3 1.245 365:17,21 365:22 1.3 361:4,20 379:16,23 1.43 399:11 1.7 364:4,8 1.75 387:18,22 1.9 364:5,8 1/15/2018 25:7 1:52 280:10 10 7:16 133:19 133:20 134:8 329:7 330:12 341:1 361:14 471:15 10:07 89:3 10:20 89:7 100 10:25 100,000 37:10 40:3 1001 4:12 100C 259:19 393:17 11 7:19 138:22
X x 1:3,12 6:8 7:1 8:1 9:1 10:1 11:1 12:1 54:12 58:12 X-axis 465:18	Y Y-axis 465:18 yeah 16:20 26:23 28:20,20 30:7,24 32:12 44:23 56:3 58:3,20,21,23 66:13 71:20 75:22,22 76:10 77:5 79:14 80:11 84:13 85:9,20 87:9 91:1 93:16,22 94:1 108:17 111:8 116:4,21 120:25 122:18 123:1 128:11 131:19 132:4 136:3 141:7 146:15 151:15 164:4 167:14	Z Zambelli-Wei... 229:11 Zazenski 11:25 438:9 443:7,9 443:16 zero 84:10 305:23 328:14 458:20,23,23 458:24,25 459:3,9,18,18 459:19,20 465:9,10,15 466:3,7,8,8,8 466:10,21 467:9 zig-zaggy 463:1 zillion 311:3	1 1 6:11 11:22 16:13,14,17 379:9 385:13 400:23 404:20 443:10 1-point 380:7 1.0 346:7 347:9 347:10,22 348:14 349:10 349:21,22,23 349:25 350:2 350:13 351:7 352:2,18,18,22 352:25 353:20 359:15,25 1.00 347:17 349:25 352:20	

138:23 139:2 11:14 151:17 11:24 151:20 110 172:6 12 7:22 8:10 213:4,4,7,9 280:22,22,23 12/14/2018 22:19 25:4 12:08 204:19 12:43 204:22 127 3:21 12th 231:12 236:1 13 8:4 235:17,18 244:7,10 246:6 247:1,16,22 248:4,10 251:4 324:4,5 325:4 325:13 326:1 133 7:18 138 7:21 14 6:3 8:11 33:1 68:9 69:12 71:8,19 87:11 244:7,10 246:6 247:1,16,22 248:4,11 251:4 267:7,8 324:4 324:6 325:4,11 325:13 326:2 328:24 414:11 14,000 36:21 1440 5:11 14807-96-6 8:13 149 172:7 14th 67:1,13 70:20,20 71:1 15 8:16 281:19 281:23 16 6:13 8:19 289:20,22 414:11 16-2738 1:5 167 121:10 147:5,12 364:20	17 4:20 6:18 8:22 296:19,23 297:14 298:5 298:22,23,23 298:24 299:19 299:21 308:22 309:16 17,103.75 25:5 18 6:22 9:4 140:3 297:17 297:18,21 298:3,10,11,11 305:6 1825 3:7 19 4:5 9:7 269:8 308:6,7,25 19103-69896 5:6 1961 285:9 1976 286:1 1979 285:10 1982 286:1 397:23 398:6 463:14 1983 328:6,18 1986 285:9 1988 285:11 1990 117:12 1993 117:13,16 1995 42:16 43:16 1996 281:23 <hr/> 2 <hr/> 2 6:14 17:18,19 17:23,25 18:19 22:3 83:11 84:2 123:15 209:23 210:25 290:1 292:9 379:14 443:2 2.0 380:16 2.13 398:10 2.20 398:24 2.27 398:24 2.41 398:3 2.5 329:6 330:11 330:21 331:16	332:15 333:18 334:9 339:24 340:16 343:16 344:14,23 347:6 2.61 398:15 2.73 398:11 2.75 398:2 2.8 11:4 394:5 396:21 397:14 399:14 2.82 398:15 2/12/2019 25:10 2/25 21:20 22:11 22:13 2:04 280:14 2:44 320:18 2:53 320:21 20 9:12 23:8 25:16 276:15 311:24 312:5,9 361:14 379:15 380:20 418:4,9 445:6,7,9 474:16 20,973.75 25:13 200 121:18 124:8,15 144:24 145:12 458:9,18 2000 5:5 361:3 394:3 463:6,9 463:16 20004 4:13 20004-1454 5:19 20005 5:12 20006 3:9 2001 400:25 2003 43:15 45:10 2004 11:24 438:8,25 439:4 441:10,14 2005 398:13 2006 261:13 378:5 394:3 2007 347:16	399:8 2008 369:8,15 390:12 398:18 425:13,14 2009 346:17 390:13 201 4:20 2010 259:7 2011 388:18 390:12 2012 259:19 388:15,19 389:3,14,24 390:6,14,19 2013 463:18 2014 11:22 139:13 346:15 431:23 2015 366:2 2016 295:19 296:10,12 2017 29:4,5 55:22 56:6,12 92:6,10 108:13 121:9,13 142:25 150:19 163:14 185:7 185:16 242:3 2018 8:15 67:1 67:13 68:9 69:13 70:21 71:1,8,19 197:3,6 271:17 359:23 364:13 424:4 2019 1:17 8:10 13:6 21:13,16 22:6 121:15 140:17 208:5 236:1 264:11 296:15,19,24 297:23 298:15 305:10 308:19 315:10 374:17 427:19 470:17 471:15 202 3:10 4:14	5:13,20 21 9:15 123:15 271:10,13,14 276:15 277:15 324:17,18,24 325:24 327:10 327:19 346:3,9 21204 2:7 213 7:24 215 5:7 219 400:21 22 9:19 233:22 234:14 236:16 237:17 327:23 327:24 328:5 22,000 36:20 226 172:8,15 22nd 140:17 23 10:4 20:19 343:3 366:11 231 45:13 232-5507 4:14 235 8:10 24 10:8 280:22 349:19 369:16 25 10:13 23:8 25:17 308:19 325:6,11,13 345:4,16 377:16 253 393:20,22 393:23 396:19 397:15 254 396:21 397:15 256 394:6 25th 21:13,16 22:6 208:4 264:11 26 10:19 377:16 393:3,10 267 8:15 27 10:23 290:22 392:25 393:1 393:14 2738 13:13 28 11:4 140:3
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276:15 277:14 396:25 397:1,4 281 8:18 289 8:21 29 11:8 413:23 414:4 297 8:23 299 9:6	36 257:12 36's 86:16 36-page 86:17 3600 420:21 366 10:7 369 10:12 37 83:9 85:9,9,9 86:23 371-7000 5:13 377 10:18,22 392 10:25 396 11:7	467 6:5 48 85:1,7 87:11 257:12,13 485 23:13 24:2,6 177:18,23	700 3:8 72 257:13 720-1288 4:7 73 296:24 400:25 732 3:23 747-9003 3:23 783-6400 3:10
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3 6:19 18:15,20 18:24 20:4 21:14 22:3 76:7 123:16 325:6 3.5 389:6 3/15/19 22:20 3/15/2019 23:2,6 3:09 338:13 3:10 338:17 3:50 377:9 30 11:12,23 45:21 46:2 181:19 269:11 379:16 380:20 416:18,19 438:25 472:12 30(b)(6) 81:23 308 9:11 30th 438:8 31 11:15 181:20 233:22 234:14 236:16 237:17 427:4,5 312 9:14 316 3:15 32 11:20 349:8 431:14,17,18 437:23 324 9:18 32502 3:16 327 9:22 33 11:23 437:19 437:21,22 34 12:4 376:25 442:19,22 35,375 25:11	4 6:23 44:20 45:2 243:6 4:10 377:12 4:59 426:16 40 45:21 46:2 298:17 299:11 391:9 457:12 400 23:13,16,24 24:19 25:17 177:22 178:7,7 458:10,18 401 4:11 41 85:8,19 413 11:11 416 11:14 42 256:5 427 11:19 43 301:9,16 309:10 310:14 431 11:22 435-7000 3:17 437 11:25 438 284:16,17 439 283:22 284:16,18 285:1 44 6:24 442 12:6 45 416:24,25 417:1 46 85:12 463-2400 5:20 465 6:4	5 7:4 35:13 52:7 52:10,11,21,25 54:4,7 122:18 243:8 349:21 433:3,3 5,068.02 25:8 5:12 426:19 5:30 447:10 5:37 447:13 5:53 464:12 5:58 464:15,19 5:59 464:22 50 156:1,2 50,000 197:16 197:23 500 458:12 51 170:11 172:5 212:3 336:18 5129 471:19 52 7:5 53 85:12 58 172:5	8 7:11 95:11,13 95:14 100:9,10 8:58 1:18 13:7 800 306:22 307:17,18 312:1,6 313:23 82 7:7 222:14 85 25:18 178:1 178:10 850 3:17 89 285:21
		<hr/> 6 <hr/>	<hr/> 9 <hr/>
		6 7:6 76:9 82:8,9 86:14 123:1 244:14 359:25 6:04 470:16,21 609 4:22 61 289:20	9 1:17 7:14 98:23,24 101:20 9:03 19:10 9:04 19:13 9:25 44:15 9:27 44:18 903 2:6 13:9 91 7:10 92 285:21 92660 4:6 94 350:18 949 4:7 95 7:13 975 5:18 98 7:15 986-1104 4:22 988-2706 5:7 99 385:13 9th 4:11 13:6 470:17
		<hr/> 7 <hr/>	
		7 7:8 26:2 28:24 29:12 31:13 34:4 42:15,22 42:24 43:2,5 43:10 91:4,5 121:5 325:10 345:5,5,17 70 286:1	

Exhibit 12

ORIGINAL ARTICLE

Uterine contractility and directed sperm transport assessed by hysterosalpingoscintigraphy (HSSG) and intrauterine pressure (IUP) measurement

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Acta Obstet Gynecol Scand 2004; 83: 369–374. © Acta Obstet Gynecol Scand 83 2004

Background. Uterine peristalsis sustains sperm transport and can be detected by hysterosalpingoscintigraphy (HSSG). This study is the first to be designed to investigate utero tubal transport function by HSSG and uterine contractility by intrauterine pressure measurement (IUP) consecutively on the same day in the periovulatory phase.

Methods. Twenty one female subjects (mean age 28.4 years) without a gynecologic history were examined sequentially by HSSG and IUP on the same day to evaluate uterine contractility in relation to the utero tubal transport function. In HSSG, intact transport function was visualized by the rapid uptake of ^{99m} technetium marked albumin aggregates through the female genital tract. In IUP, the frequency of uterine contractions (UC/min), amplitude of uterine contractions and basal pressure tone were detected via a intrauterine catheter. HSSG and IUP were embedded in cycle monitoring with measurement of LH and estradiol.

Results. In HSSG, a positive transport of inert particles was assessed in 20 of 21 subjects, in 76% to the side of the dominant follicle or on both sides of the oviduct, and in 19% a strict contralateral transport could be observed. In only one subject (5%), no transport was assessed. The mean value of uterine contractions was 3.4 UC/min (SD ± 0.7), the mean amplitude was 12.0 mmHg (SD ± 4.25 mmHg). Basal pressure tone was 70.7 mmHg. There was a statistically significant correlation with estradiol levels: none of the subjects with less than 3 UC/min showed an estradiol level higher than 100 pg/mL; nearly every patient (one exception) with more than 3 UC/min had an estradiol level higher than 100 pg/mL ($p < 0.0001$, Fisher's exact test).

Conclusions. Intact periovulatory utero tubal transport function can be documented by HSSG and is caused by directed uterine contractility, measured consecutively by IUP. Uterine contractility is influenced by rising estradiol levels. Directed uterine contractility and intact utero tubal transport function are considered necessary for intact sperm transport, mainly to the side bearing the dominant follicle to maximize fertility.

Key words: intrauterine pressure; intrauterine contractility; HSSG; utero tubal transport function

Submitted 23 June, 2003
Accepted 8 September, 2003

Uterine peristalsis is of critical importance in the process of reproduction and has been investigated mainly by transvaginal ultrasound examination (1,2). Uterine peristalsis only

involves the stratum subvasculare of the myometrium and reveals cyclic changes in direction, frequency and intensity (3,4). During menstruation, contraction waves with the lowest

frequency are directed towards the cervix, while during the other phases of the cycle, with the highest frequency and intensity during the periovulatory phase, cervico-fundal peristalsis prevails (3,5). Uterine contractions are involved in the expulsion of menstrual debris as well as in rapid directed sperm transport (6–9) and in the high fundal implantation of the embryo in the luteal phase.

Two methods have generally been used to assess uterine contractions (UC): one involves a record of changes in intrauterine pressure (IUP) using invasive probes that detect intraluminal variation of pressure produced by the UC (10–12). A less invasive technique has been invented in various forms of direct visualization of UC with transvaginal ultrasound, some from digitized scans. Ultrasound measurements usually provide information on the direction of UC propagation, which is difficult to detect in IUP recordings. In contrast, IUP measurement allows a quantification of the UC amplitude, especially in the periovulatory period.

Hysterosalpingoscintigraphy (HSSG) (13,14) can be used to investigate the utero-tubal transport mechanism of the female genital tract *in vivo* by means of technetium-labeled albumin macro-spheres of the size of sperm that are placed in the posterior vaginal fornix. The ascension of these particles within the female genital tract can be observed by scintigraphy.

In this study, to our knowledge, this is the first time that uterine contractions have been measured in frequency and amplitude by IUP in the late follicular phase, and consecutively correlated with the utero-tubal transport mechanism assessed by HSSG on the same day.

Material and methods

Twenty one healthy patients (mean age 28.4 years) with a history of fertility or infertility due to severe andrologic factors were examined by HSSG and measurement of the IUP on the same day in the late follicular phase. All patients had ovulatory cycles and underwent a monitored cycle when HSSG and IUP were performed. Both examinations were undertaken successively on the same day. Ovulation was proven by an LH surge. All patients had proven patency of fallopian tubes by chromolaparoscopy or hysterosalpingosonography.

Exposure of the ovaries to radiation was calculated to be 0.8–1.4 cGy, with the mean exposure below a threshold of 1 cGy. By comparison, radiation exposure in the standard procedure of hysterosalpingography (HSG) is more than seven times higher, at 7.6 cGy.

The study was approved by the local ethics committee and patients gave their informed consent about HSSG and IUP and were strictly advised not to become pregnant during the diagnostic cycle in which HSSG was carried out.

HSSG

HSSG is a well established technique for evaluating the utero tubal transport mechanism (7–9). The examination was performed as close as possible before ovulation in the late follicular phase. On the day of the examination, the size and the location of the dominant follicle were detected ultrasonographically. For HSSG, 10 MBq ^{99m}Tc technetium marked macroalbuminaggregates (Solco MAA; Solco Basel AG, Birsfelden, Switzerland) with a size of 5–20 μm , which imitates the size of sperms, were diluted with 2 mL saline solution 0.9% and then administered in the posterior vaginal fornix of the supine patient. Serial scintigrams were taken by a gamma camera. For quantitative evaluation of HSSG, 'regions of interest' (ROI) were determined in the area of both fallopian tubes to visualize the concentration of radioactivity in the area of the oviduct. By using ROIs, radioactivity can easily be attached to the compartment's uterine cavity or fallopian tubes. Taking into account the size and location of the dominant follicle, the results of HSSG can be classified as follows:

Ipsilateral: concentration of radioactivity on the side of the dominant follicle.

Contralateral: concentration of radioactivity on the opposite side of the dominant follicle.

Both sides: equal concentration of radioactivity on both sides.

No tubal transport (uterine cavity): concentration of radioactivity in the area of the uterine cavity without any further transport to the fallopian tubes.

IUP

Each of the 21 women underwent IUP measurement directly after HSSG. IUP was recorded as follows: a rubber balloon catheter (Ruesch 5 Ch., Ruesch AG[®], Kernen, Germany) for intrauterine use was gently inserted into the uterine cavity and blocked with 0.5 mL of distilled water. Its hollow cavity was filled with sterile distilled water so that uterine contractions could easily be transferred to a transducer calibrated to convert mechanical to electrical signals. In none of the patients was cervical dilatation necessary, nor was a tenaculum used. Storage of data followed on a PC with specifically designed software (ScopeView, Metex[®]). The exact position of the rubber balloon was estimated in the lower third of the uterine cavity and controlled by transvaginal ultrasound. Recordings lasted 15–20 min.

In every patient the frequency of uterine contractions could be calculated by the number of oscillations per minute and expressed as the number of uterine contractions per minute (UC/min). The amplitude of contractions was expressed in mmHg and defined as the difference from the baseline pressure tone. Basal pressure tone was also detected in mmHg and expresses the basal myometrial activity in the late follicular phase.

In every patient LH and estradiol were measured on the day of the examination.

Documentation of data and statistical analysis was performed with SPSS for windows (SPSS Inc., Chicago, Illinois, USA) on a PC. Statistical significances were calculated with Fisher's exact test. A *p* value <0.05 was considered to be statistically significant.

Results

HSSG

In 16 of 21 (76%) patients an ipsilateral positive transport to the side of the dominant follicle or transport towards both oviducts could be

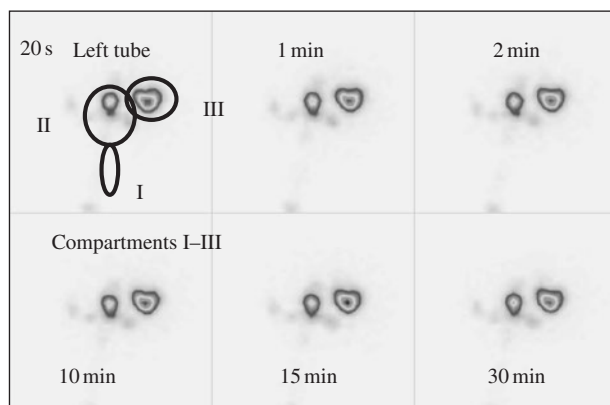


Fig. 1. Hysterosalpingoscintigraphy: demonstration of radio activity on the left side with a dominant follicle of 15 mm in diameter (ipsilateral demonstration). Compartment I, vagina; compartment II, uterine cavity; compartment III, oviduct. Positive transport mechanism can easily be detected in an early scan after 20 s.

observed (Fig. 1). In four patients (19%) the positive transport could be documented strictly on the contralateral side, in one patient (5%) no tubal transport could be observed (negative transport function). In summary, 20 of the 21 evaluated subjects had a positive transport function of the utero-tubal unit, sustained by uterine contractions. One patient showed a dominant follicle of 17 mm in diameter, an estradiol level of 125 pg/mL, and a contraction of 4.07 UC/min, but failed to build up an intact transport mechanism.

IUP

In all patients uterine contractions could be easily observed (Fig. 2). The IUP measurement took place in the periovulatory phase directly following HSSG on the same day. Contractions varied between 1.8 and 5 UC/min.

The mean value of contractions in the periovulatory phase was 3.4 UC/min (SD ± 0.7).

The amplitude of contractions varied in range from 8 to 36 mmHg. The mean amplitude was 12.0 mmHg (SD ± 4.25 mmHg).

The basal pressure tone of the uterus reflects the basal isotonic contraction of this strong muscle containing smooth muscle fibers. In our patients the basal muscle tone was 70.7 mmHg (SD ± 15.7 mmHg) in the periovulatory phase (Table I).

Depending on the estradiol levels, uterine contractility reveals a statistically significant increase: none of the patients showing less than 3 UC/min had an estradiol level higher than 100 pg/mL (mean 63 pg/mL). By comparison, nearly every patient (one exception) with more than 3 UC/min had an estradiol level higher than 100 pg/mL (mean 201 pg/mL) (Table II, $p < 0.0001$).

Discussion

Rhythmic contractions of the nonpregnant uterus have been demonstrated by invasive techniques in

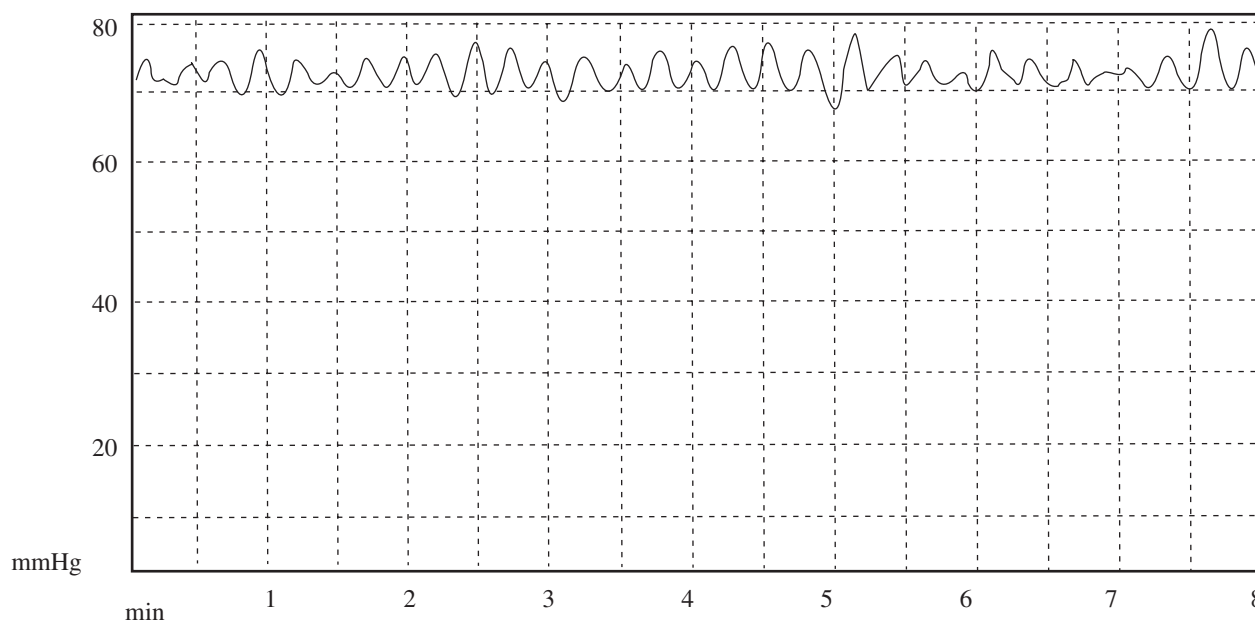


Fig. 2. Contractility pattern demonstrated by IUP in the same patient (see Fig. 1). The patient showed a dominant follicle of 15 mm on the left side, LH peaked on the day of the examination, and the estradiol level was 120 pg/mL. A mean contractility of 3.3 UC/min was detected, with a mean pressure amplitude of 14.1 mmHg and the basal tone was 73.3 mmHg.

Table I. Results from intrauterine pressure measurement ($n = 21$) in the periovulatory phase

	Mean	Range
Frequency (UC/min)	3.4 (± 4.25)	1.8-5.0
Amplitude (mmHg)	12.0 (± 4.25)	8.0-36.0
Basal tone (mmHg)	70.7 (± 15.7)	36.0-96.7

different species including humans (10–12). From the end of menstruation until the late proliferative phase most researchers found small and frequent contractions in a retrograde direction (cervico-fundal). The main interest in these first studies was to evaluate uterine contractility during menstruation, which revealed slower and stronger contractions in an antegrade (fundo-cervical) direction.

Before the noninvasive technique of trans-abdominal or transvaginal ultrasonography appeared, the reasons for propagated uterine contractions in the late follicular phase remained enigmatic. Transvaginal studies (3–5) demonstrated a tremendous cyclic increase in frequency and amplitude of uterine contractions towards the fundus uteri throughout the late follicular phase and the periovulatory phase. This contractility pattern was reversed in the luteal phase. The authors presumed that these subendometrial contractions could be of importance concerning sperm transport.

Kunz et al. (8) reported for the first time a direct relationship between the increase in the frequency of uterine contractions assessed by transvaginal ultrasound and the percentage of ipsilateral transport of sperm-like material by HSSG. The mean value for uterine contractions in the preovulatory phase was constantly considered to be in the range 2.8–3.0 UC/min. This process was positively correlated with increasing estradiol levels, but the intrauterine pressure has not been recorded because of its invasive character. Nowadays, HSSG has been established for evaluating the integrity of the utero-tubal transport function (7–9,13,14).

Based upon the encouraging results of these studies, Kadanali et al. (6) reported similar results concerning utero-tubal transport capacity when

radioactive-labeled sperm were used compared to 99m -technetium-marked albumin macrospheres in patients bearing an intrauterine device (IUD) *in vivo*.

Therefore, there is even *in vivo* substantial evidence that the utero-tubal transport unit is responsible for intact sperm transport.

Contradictory results have also been published (15), although no information was given about the size and location of the dominant follicle and the estradiol levels of the patients examined. The majority of authors working with HSSG support this method as an important diagnostic tool for infertility workup.

To our knowledge, our study is the first to provide proof of an intact sperm transport mechanism assessed by HSSG in healthy women directly followed by IUP measurement. IUP recordings reveal strong and high-frequency contractions that are responsible for the integrity of the utero-tubal transport system.

Although we were not able to investigate the direction of the contraction waves by using only one inserted catheter, the aim of this study was to examine the amplitude, frequency and basal pressure tone in the decisive reproductive phase of the menstrual cycle, results that cannot be obtained by ultrasonographic examination alone.

Uterine contractility at various phases of the menstrual cycle by transvaginal ultrasound and IUP recordings on the same day was first published by Bulletti et al. (16). There was no difference between the measurement of ultrasonographic contractions and contractions measured by IUP recordings, which were 2.9 UC/min in the late follicular phase and 3.9 UC/min in the periovulatory phase. However, IUP recordings were only taken in five subjects.

Our data concerning uterine contractility measured by IUP confirm, in a higher number of subjects, the findings of Bulletti et al., who found a mean value of 3.9 UC/min in the periovulatory phase. Our data revealed 3.4 UC/min at that phase of the cycle. The only difference between the findings is a lower amplitude of uterine contractions (12.0 vs. 25.6 mmHg) and a higher basal tone (70.7 vs. 56.2 mmHg) in our patients. The higher basal tone might be due to the influence of the rubber balloons on the calculated tone pressure.

Failure of an intact utero-tubal transport function as assessed by negative HSSG (no tubal transport) (17) is associated with poor pregnancy rates and might reflect a dissynchronization of uterine wall movements (18).

We found a statistically significant relationship between rising estradiol levels and an increase in UC/min. None of our patients showed less than

Table II. Dependence of uterine contractility on estradiol levels ($n = 21$)

Frequency (UC/min)	Estradiol	
	<100 pg/mL (mean 63 pg/mL)	>100 pg/mL (mean 201 pg/mL)
<3	8	0
≥ 3	1	12

3 UC/min if the estradiol level was higher than 100 pg/mL. This observation indicates that the integrity of utero-tubal transport function transport through the female genital tract is under the endocrine control of the dominant follicle.

As an outlook for further investigations, it would be interesting to perform IUP recordings in patients with endometriosis, as endometriosis and adenomyosis uteri can be regarded as a unique disease the dislocation of the basal endometrium (19), which is linked with hyper- and dysperistalsis and impeded transport function in HSSG (20). There are data suggesting a higher basal tone of the uterus in patients with endometriosis (21). In patients with endometriosis, a high percentage of structural uterine wall abnormalities are described in transvaginal ultrasonography as well as in T2-weighted magnetic resonance imaging (MRI) (22).

Concerning uterine contractility, patients with endometriosis show a higher frequency, amplitude and basal pressure tone in IUP during menstruation than healthy controls (23). This confirms the results by transvaginal ultrasonography that patients with endometriosis predominantly show a retrograde contractility pattern (in the cervico-fundal direction) (24). These studies might indicate that an increase of cervico-fundal peristalsis might increase the amount of dislocated basal endometrium for intraperitoneal implantation.

Medical treatment studies to reduce uterine contractility are mainly performed in pregnant patients (25,26) but would certainly be of value in reducing dysregulated uterine contractility in patients with endometriosis.

To summarize, our data provide proof that uterine contractility with a mean value of 3.4 UC/min is under the control of the hormonal cycle and regulates the intact uterine transport function assessed by HSSG.

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374 *S. Kissler et al.*

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Exhibit 13

THE UTERINE PERISTALTIC PUMP

Normal and Impeded Sperm Transport within the Female Genital Tract

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1. SUMMARY

Rapid as well as sustained sperm transport from the cervical canal to the isthmic part of the fallopian tube is provided by cervico-fundal uterine peristaltic contractions that can be visualized by vaginal sonography. The peristaltic contractions increase in frequency and presumably also in intensity as the proliferative phase progresses. As shown by placement of labeled albumin macrospheres of sperm size at the external cervical os and serial hysterosalpingoscintigraphy (HSSG) sperm reach, following their vaginal deposition, the uterine cavity within minutes. In the early follicular phase a large proportion of the macrospheres remains at the site of application, while a smaller proportion enters the uterine cavity with even a smaller one reaching the isthmic part of the tubes. In the mid-follicular phase of the cycle with increased frequency and intensity of the uterine contractions the proportion of macrospheres entering the uterine cavity as well as the tubes has significantly increased. In the late follicular phase with maximum frequency and intensity of uterine peristalsis the proportion of macrospheres entering the tube increases further at the expense of those at the site of application as well as within the uterine cavity. The transport of the macrospheres into the tube is preferentially directed into the tube ipsilateral to the dominant follicle, which becomes apparent in the mid-follicular phase as soon as a dominant follicle can be identified by ultrasound. Since the macrospheres are inert particles the directed sperm transport into the tube ipsilateral to the dominant follicle is not

functionally related to a mechanism such as chemotaxis but is rather provided by uterine contraction of which the direction may be controlled by a specific myometrial architecture in combination with an asymmetric distribution of myometrial oestradiol receptors.

Women with infertility and mostly mild endometriosis display on VSUP a uterine hyperperistalsis with nearly double the frequency of contractions during the early and mid- as well as midluteal phase in comparison to the fertile and healthy controls. During midcycle these women display a considerable uterine dysperistalsis in that the normally long and regular cervico-fundal contractions during this phase of the cycle have become more or less undirected and convulsive in character. Hyperperistalsis results in the transport of inert particles from the cervix into the tubes within minutes already during the early follicular phase, and may therefore constitute the mechanical cause for the development of endometriosis in that it transports detached endometrial cells and tissue fragments via the tubes into the peritoneal cavity. Moreover, dysperistalsis may contribute to the infertility in these patients since it results in a break down of sperm transport within the female genital tract.

2. INTRODUCTION

There is no doubt that the ultimate fate of the successful male germ cell is to impregnate the female oocyte, where its genetic material will fuse with that of the oocyte to result in fertilization and embryo formation. This particular sperm is usually deposited five to zero days prior to ovulation (Wilcox *et al.*, 1995) in the posterior vaginal fornix in close vicinity to the external os of the cervical canal from where it reaches its final site of destination, the place of sperm-oocyte encounter within the tube ipsilateral to the dominant follicle.

Usually, the uterus is considered to be specialized, first, for the reception of the blastocyst by the endometrium and the continuous nourishment of the developing fetus and, second, for the eventual expulsion of the fetus (Romanini, 1994). Considering the fact that the sperm has to cover a long distance within the female genital tract from the external os of the cervix to the site of fertilization within the tube it is surprising that the facilitation and the guidance of this journey has only recently been considered a genuine and active function of the uterus (Kunz *et al.*, 1996a). Previously, the ascension of the sperm within the female genital tract to the site of fertilization was regarded more or less a functional capacity of the sperm itself with the uterus serving merely as a passive canal, although a functional importance had been ascribed to uterine contractions (Moghissi, 1977; Harper, 1994). With respect to sperm ascension, attention was mostly directed towards the cervical canal with its glands and cyclically changing secretion. These are assumed to provide optimal conditions for the penetration of the sperm into the female genital tract around ovulation and serve, with its crypts, as a sperm reservoir, from where constant release for sustained sperm transport could occur. In this communication, the mechanism of uterine peristalsis will be discussed, and its role in sperm transport within the female genital tract will be outlined. It will be demonstrated that this function of the uterus is of fundamental importance in the process of reproduction and that disturbances of the uterine mechanism of sperm transport may result in infertility.

3. UTERINE PERISTALSIS

Rapid sperm transport from the vagina to the Fallopian tubes within minutes has been described in many species including man (Hartman, 1962; Mortimer, 1983; Hunter,

1987; Drobnis and Overstreet, 1992; Harper, 1994). Since the velocity of sperm movement does not itself account for covering such a long distance through the female genital tract within a few minutes, rapid sperm transport is considered a passive phenomenon and has been ascribed to uterine contractions (Moghissi, 1977; Harper, 1994; Kunz et al., 1996a; Leyendecker et al., 1996).

3.1. Vaginal Sonography of Uterine Peristalsis (VSUP)

Contractile activity of the non-pregnant uterus has been known for many decades (Hendricks, 1966; Cibils, 1967; Martinez-Gaudio et al., 1973). High resolution sonography has made it possible to demonstrate these contractions without invasive techniques. These contractions involve mostly the subendometrial layer of the myometrium and may be detected only by endometrial movements (Birnholtz, 1984). Following their first description they have been further characterized (Oike et al., 1988; De Vries et al., 1990; Lyons et al., 1991; Fukuda and Fukuda, 1994). The contractions increase in frequency and in intensity as the follicular phase progresses with an inverse pattern during the luteal phase. The peristaltic waves of the endometrium and the subendometrial layer of the myometrium are directed from the cervical canal to the fundal part of the uterus, while only during menstruation do they exhibit a fundo-cervical direction (Lyons et al., 1991).

In our own study (Kunz et al., 1996a; Leyendecker et al., 1996), with measurements of the uterine peristalsis during the menstrual period, the early, mid- and late follicular as well as mid-luteal phases of the cycle, respectively (Fig. 1) it was demonstrated that there was a steady increase in peristaltic activity ranging from roughly 1.2 contraction per minute during the menstrual period and early follicular phase to 2.8 contractions per minute in the late follicular phase. During the mid-follicular and mid-luteal phases, respectively, the frequency averaged 1.5 contractions per min. Over the same time period, the proportion of fundo-cervical contraction waves decreased significantly from 43% during the menstrual period to less than 1% in the periovulatory phase. Thus, almost all peristaltic

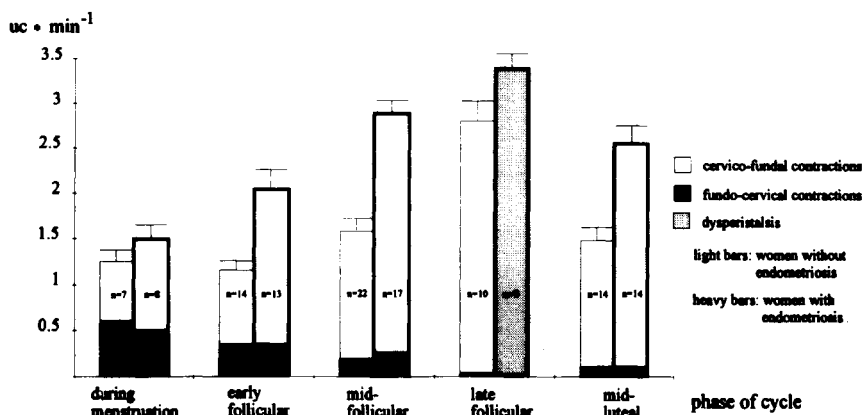


Figure 1. A graphical demonstration of the frequency of the subendometrial uterine peristaltic waves during menstruation, the early, mid- and late follicular and mid-luteal phases of the cycle, respectively, as determined by vaginal ultrasonography (contractions/min \pm SEM). The graph shows also the relative distribution of fundo-cervical contractions versus cervico-fundal contractions during these different phases of the cycle (from Leyendecker et al., 1996).

waves of the uterus during the late follicular phase had a cervico-fundal direction. They also appeared to be more intense than during the other parts of the follicular phase, which might, however, be related to the thickness of the endometrium rendering the movements more pronounced. In comparison to the early follicular phase, however, a thicker proportion of the myometrium appeared also to be involved in the contractions. Because the frequency, intensity and direction of the uterine peristalsis depend upon the phase of the cycle, an endocrine control of this phenomenon by the ovary may be assumed. In this regard oxytocin and prostaglandins may function as mediators (Eliasson and Posse, 1960; Hein *et al.*, 1973; Karim *et al.*, 1973; Fuchs *et al.*, 1985; Lefebvre *et al.*, 1994a, Lefebvre *et al.*, 1994b). This view is supported by the finding that administration of oestradiol valerate to hypogonadal women yielding a pattern of serum oestradiol values similar to that of the normal cycle could completely mimic the cyclic changes of uterine peristalsis and that the frequency of the uterine peristaltic contractions could be significantly increased during the follicular phase of the cycle by the administration of an i.v. bolus of oxytocin. The increase in the frequency of the peristaltic contractions could be totally attributed to the peristaltic waves with cervico-fundal direction, which may be related to the high density of oxytocin receptors in the cervical tissue (unpublished).

Peristaltic contractions with the same frequency as described above were also observed with transvesical scanning (Birnholtz, 1984). Thus, it is very unlikely that the uterine peristalsis was induced by the vaginal ultrasound examination. In contrast, it can be assumed that uterine peristalsis during the menstrual cycle is a continuous phenomenon with varying frequency, intensity and direction of the contraction waves depending on the phase of the cycle and does not require a specific stimulus for initiation. These studies, however, do not exclude a coital enhancement of uterine contractions.

3.2. Hysterosalpingoscintigraphy (HSSG)

It is reasonable to assume that the uterine peristaltic activity provides the forces that are required for the transport of spermatozoa from the external os of the cervix into the tubes within minutes. Using hysterosalpingoscintigraphy (Itturalde and Venter, 1981; Becker *et al.*, 1988), rapid sperm transport was studied by placing technitium-labelled albumin macrospheres of sperm size at the external os of the uterine cervix and following their path through the female genital tract (Kunz *et al.*, 1996a; Leyendecker *et al.*, 1996). The albumin macrospheres used in our study resemble spermatozoa in their size. Thus, the demonstration of their ascension through the genital was considered to represent passive sperm transport.

According to these data (Fig. 2–4) the following concept of the dynamics of rapid sperm ascension within the female genital tract was proposed. Rapid sperm ascension occurs immediately following deposition of the ejaculate at the external os of the cervix. As early as one minute thereafter spermatozoa have reached the intramural and isthmic part of the tube. Quantitatively, however, the extent of ascension increases with the progression of the follicular phase. While only a few spermatozoa enter the uterine cavity and even fewer the tubes during the early follicular phase, the proportion of spermatozoa that enters the uterine cavity increases dramatically during the mid-follicular phase with still a limited entry into the tube. During the late follicular phase there is a considerable ascension of spermatozoa into the tubes.

Furthermore the HSSG revealed the preferential direction of rapid sperm transport into the tube ipsilateral to the dominant follicle. This corresponds with recent findings during surgery that the number of sperm around ovulation was higher in the tube ipsilat-

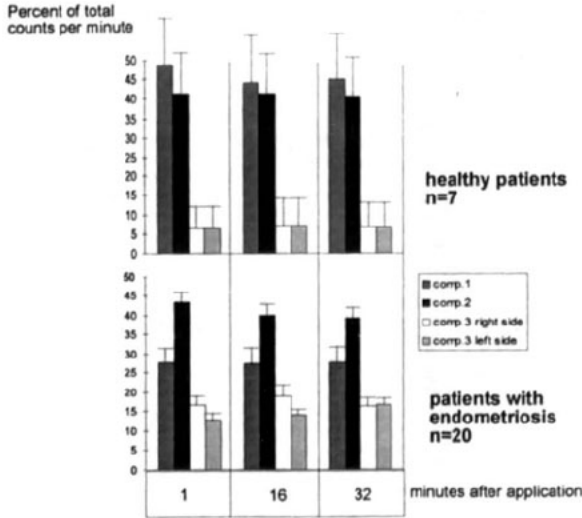


Figure 2. The distribution of the percentage of total counts, representing the labeled albumin microspheres, within the female genital tract (compartment 1, 2 and 3 being the upper vagina, the uterine cavity and the isthmic part of the tubes respectively) following 1, 16 and 32 minutes after vaginal application during the early follicular phase. With respect to compartment 3, the right and left tubes were differentiated. The amount of radioactivity transported into the tubes was significantly higher in patients with endometriosis in comparison with healthy controls ($P < 0.01$) (from Leyendecker et al., 1996).

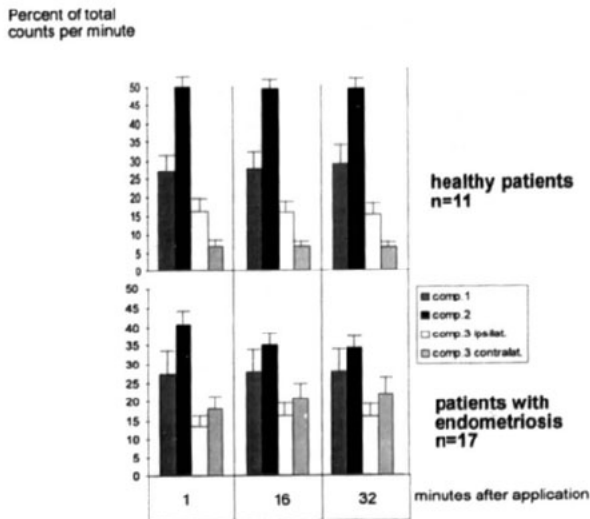
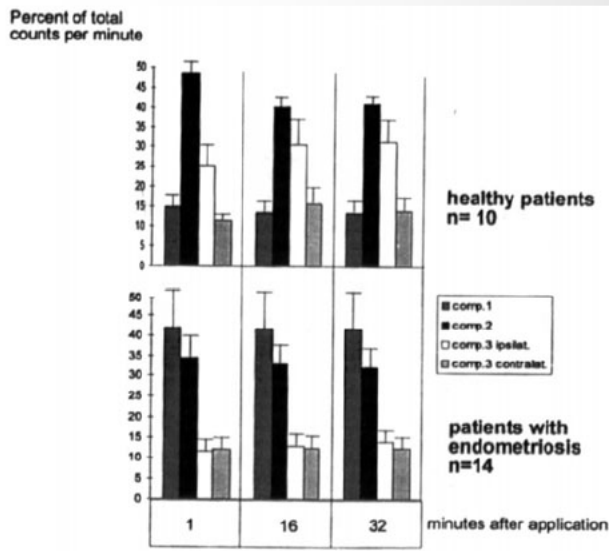


Figure 3. The respective distribution pattern of radioactivity, as in Fig. 2, obtained during the mid-follicular phase of the cycle. While in patients without endometriosis the labeled microspheres preferentially entered the tube ipsilateral to the dominant follicle, in patients with endometriosis the microspheres preferentially entered the tube contralateral to the dominant follicle. The difference in ascension into the contralateral tube between the two groups of patients was significant ($P < 0.01$) (from Leyendecker et al., 1996).



by the dominant follicle in that the uterine myometrium with its specific architecture (Goerttler, 1930) is activated and contracts in a manner providing this directed transport. In order to elucidate the mechanisms that govern directed sperm ascension, the estrogen receptor distribution within the myometrium was studied. It could be demonstrated in removed uteri that the percentage of estrogen receptor positive nuclei of smooth muscle cells in the myometrium was significantly higher on the side of the dominant ovarian structure in comparison with the contralateral side (Kunz et al., 1996b).

The strong correlation between receptor distribution and the site of the dominant ovarian structure suggested that the side-specific asymmetric estrogen receptor distribution is induced by the dominant follicle. This preferential induction of estrogen receptors in the myometrium on the side of the dominant ovarian structure is presumably not effected by the oestradiol concentration in the systemic circulation. Rather, it may involve a more direct endocrine influence mediated, for example, by the utero-ovarian vascular counter-current system (Einer-Jensen, 1988) that may provide higher oestradiol concentrations in the uterus on the side of the dominant follicle. This finding may also indicate that other hormone receptors in the uterus, pertinent to its contractile function, might be expressed asymmetrically with respect to the localization of the dominant ovarian structure. Preliminary data show that oxytocin receptors, exhibiting high concentrations in cervical tissue, like those for oestradiol, are asymmetrically distributed within the fundal part of the myometrium relative to the side of the dominant follicle (unpublished).

The asymmetric estrogen receptor distribution being presumably responsible for the directed sperm transport appears to be superimposed on a basal, more evenly distributed level of estrogen receptors under the influence of systemic oestradiol. This may be derived from the observation that the systemic administration of exogenous estrogen to hypogonadal women results in a uterine peristaltic activity which is, according to VSUP, indistinguishable from normal

5. UTERINE HYPERPERISTALSIS AND DYSPERISTALSIS

In studying infertile women suffering from mostly mild endometriosis, which is considered not to be a cause of infertility (Hull et al., 1986; Adamson and Pasta, 1994), a fundamental disturbance of uterine peristaltic activity was observed (Leyendecker et al., 1996) (Fig 1). In VSUP, these women displayed a considerable degree of hyperperistalsis in that, during the early and mid follicular as well as mid-luteal phase of the cycle, respectively, the frequency of peristaltic contraction was nearly doubled in comparison to normal. During the late follicular phase the frequency was increased further but less pronounced as compared to the early and mid-follicular phase of the cycle. The character of the peristaltic activity, however, had completely changed. While in the fertile controls long and regular cervico-fundal peristaltic waves prevailed, the contractions displayed a convulsive character in the infertile women. Some of the contraction waves started in the middle portion of the uterine cavity, while in other patients the contractions started at different sites at the same time, and some vanished before reaching the fundal part of the uterine cavity. Thus, in comparison with the regular and frequent cervico-fundal contractions of healthy women, the impression of a dysperistalsis prevailed in patients with infertility and endometriosis (Leyendecker and Kunz, 1996).

These abnormalities of the uterine peristaltic activity in women with endometriosis had a profound impact on the uterine transport function as demonstrated by HSSG, which, at least in part, may account for the infertility of these women. Already during the early

follicular phase of the cycle, there was a rapid transport of inert particles through the uterine cavity into the tubes. This was further increased during the mid follicular phase. However, there was no directed transport into the tube ipsilateral to the dominant follicle. During the late follicular phase, when the uterine contractions had become dysperistaltic, a breakdown of the uterine transport function occurred in that most of the particles remained at the site of application and only a few entered the tubes without a preference for the "dominant" one (Fig. 2-4).

6. IMPLICATIONS REGARDING THE FUNCTION OF THE CERVICAL MUCUS

These data are also pertinent in reconsidering some of the functions of the cervical mucus with regard to sperm ascension.. It is generally assumed that the sperm actively penetrate the cervical mucus and that the scant and viscous cervical mucus of the early follicular phase acts as a barrier in this respect (Moghissi, 1977). The HSSG demonstrates that already in the early follicular phase, in the presence of scant cervical mucus with little spinnbarkeit, a rapid transport of inert particles through the cervical canal occurs (Fig 2). Moreover, the distribution pattern of the labeled macrospheres within the genital tract of women with endometriosis and hyperperistalsis in the early follicular phase (Fig. 2; lower panel) resembles that of the healthy controls with normoperistalsis in the mid follicular phase of the cycle (Fig. 3; upper panel). Thus, it is not so much the quality of the cervical mucus but rather the power of the uterine peristalsis that determines the amount of sperm ascension through the cervical canal.

According to in vitro studies sperm penetrate the cervical mucus at a speed of 0.1 to 3 mm/min depending upon the phase of the cycle. There is no doubt on the basis of our studies that the sperm's own velocity is of little importance with respect to the ascension through the cervical canal. Irrespective of whether there is a function at all to the sperm's active movement at this stage of reproduction, the interaction of the sperm with the physico-chemical properties of the mucus enable viable sperm to enter the cervical crypts as a primary reservoir for later release. Of course, our model using inert albumin macrospheres cannot account for effects that have to be attributed to the functional capacity of healthy sperm.

7. AN INTEGRAL VIEW ON SPERM ASCENSION WITHIN THE FEMALE GENITAL TRACT AND ITS POSSIBLE DISTURBANCES

The clinician has been familiar for a long time with rhythmical contractions of the non-pregnant uterus. Upon cervical inspection during the preovulatory phase rhythmical protrusions of the abundant cervical mucus can be observed. Only recently, due to high resolution ultrasound examination, it was possible to relate these cervical activities to uterine peristaltic waves that originate in the cervix and are propagated towards the cornual section of the uterus. With the placement of labeled inert particles of sperm size at the external cervical os and following their path through the female genital tract by HSSG it was possible to demonstrate the enormous power and transport capacity of this uterine peristaltic pump. Furthermore, the directed transport of the particles preferentially into the

tube ipsilateral to the dominant follicle demonstrated the surprising sophistication of this uterine system of sperm transport (Kunz et al., 1996a).

On the basis of the data obtained in our studies and available from literature, we hypothesize that rapid as well as sustained sperm is controlled by uterine peristaltic activity. Uterine contractions aspirate sperm into the cervical mucus and the uterine cavity, and provide further transport into the isthmic part of the tubes. In the mid- and late follicular phases of the cycle this transport is directed preferentially into the tube ipsilateral to the dominant follicle. This indicates that the mechanism of rapid and passive sperm transport is under the endocrine control of the dominant follicle. Some sperm, probably the most motile ones, follow, by their own movement, the filamentous structures of the cervical mucus and enter the cervical crypts as a primary reservoir. This results in a partial sequestration of the sperm increasing the proportion of less motile and immobile sperm that reach the tubes rapidly. This observation has probably lead to the notion that rapid sperm ascension might not be essential for fertilization (Mortimer, 1983; Hunter, 1987). With the progression of the follicular phase there is an increasing release of sperm from the primary reservoir as they are flushed and squeezed out of the crypts due to the cervical secretion which becomes more profuse and the rhythmical contractions that originate within the cervix, respectively. Entering the "main stream" of cervical secretion they are caught by the "uterine peristaltic system" and rapidly transported in an aliquot of mucus (Fukuda and Fukuda, 1994), which protects the sperm from leukocyte degradation within the uterine cavity (Harper, 1994), to the tube with its isthmic mucus as the secondary reservoir. Dilatation of the external cervical os, maximum cervical secretion and rhythmical protrusion of the mucus around ovulation enlarge the zone of contact between a fresh ejaculate and the uterine peristaltic pump. At the same time preovulatory mucorrhea, together with the rhythmical contractions of the cervix, prevents by large motile sperm from entering the cervical crypts and thus ensures, in combination with maximally increased uterine peristalsis, that no or only minor sequestration of sperm can occur and that motile sperm are directly transported into the isthmic mucus (Jansen, 1980) of the tube ipsilateral to the dominant follicle where they are available for fertilization.

There is, in our opinion, no principle difference between the mechanisms of rapid and sustained sperm transport, respectively. Both aim at the availability of viable sperm at the site of fertilization around ovulation and both rely, in this respect, on the continuous peristaltic activity of the uterus. Sustained sperm transport utilizes the cervical crypts as a primary reservoir, from where later release occurs. The reduced power of the peristaltic pump several days prior to ovulation in comparison to the preovulatory phase might, together with a more viscous cervical mucus at this time, facilitate the migration of motile sperm into the cervical crypts. No data are available, which of the two reservoirs, the cervical or the tubal mucus, have a preponderance in the function of sperm preservation. If there is any preponderance at all, one may assume that it may shift from the cervix to the tube with the progression of the preovulatory phase. In any event, the fundamental importance of sperm preservation within the genital tract and sustained sperm transport for the overall process of reproduction is documented by the observation that intercourse several days prior to ovulation may result in a pregnancy with a considerable probability ranging from about 10% with intercourse five to more than 30% with intercourse two days prior to ovulation, respectively (Wilcox et al., 1995).

These data and considerations show that the availability of sperm at the site of fertilization at the appropriate time depends to a large extent on coordinated uterine peristaltic contractions that cyclically change in quality and frequency. At a low frequency and power, they may favor sperm preservation within the cervical mucus, at a higher preovula-

tory frequency and power of contractions, the uterine peristaltic pump provides rapid and directed transport of sperm either from the reservoir or from a freshly deposited ejaculate into the tube ipsilateral to the dominant follicle.

Recently, it could be shown that this fine-tuned system is fundamentally disturbed in women with infertility and, mostly, mild endometriosis. Both, the hyper- and dysperistalsis of the uterine peristaltic pump observed in these women may contribute to their reduced fertility. Hyperperistalsis may prevent the development of an adequate pool of preserved sperm within the reservoir of the cervical crypts, and preovulatory dysperistalsis impedes, by a breakdown of sperm transport, the formation of an adequate sperm reservoir in the mucus of the isthmic part of the tube from where sperm migrate to the final site of fertilization.

Independent of its effects on sperm transport and fertility uterine hyperperistalsis may promote the detachment and exfoliation of endometrial cells and tissue fragments and their transtubal transport into the peritoneal cavity and may, therefore, propagate the development of endometriosis (Leyendecker et al., 1996).

8. CONCLUSIONS

Uterine peristalsis is of fundamental importance in the process of reproduction in that it serves sperm transport from the external os of the cervix to the mucus of the isthmic part of the tube ipsilateral to the dominant follicle. This mechanism is controlled by the dominant follicle. This newly disclosed and described uterine function is of clinical importance in that a dysfunction of this functional system may result in infertility and may propagate the development of endometriosis.

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Exhibit 14

Physiology of Upward Transport in the Human Female Genital Tract

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ABSTRACT: The uterus and fallopian tubes represent a functionally united peristaltic pump under the endocrine control of ipsilateral ovary. We have examined this function by using hysterosalpingoscintigraphy (HSS), recording of intrauterine pressure, electrohysterography, and Doppler sonography of the fallopian tubes. An uptake of labeled particles into the uterus was observed during the follicular and luteal phases of the cycle after application into the vagina. Transport into the oviducts, however, could only be demonstrated during the follicular phase. Furthermore, the predominant transport was into the tube ipsilateral to the ovary containing the dominant follicle. The pregnancy rate following spontaneous intercourse or insemination was higher in those women in whom ipsilateral transport could be demonstrated. The amount of material transported to the ipsilateral tube was increased after oxytocin administration, as demonstrated by radionuclide imaging and by Doppler sonography following instillation of ultrasound contrast medium. An increase in the basal tone and amplitude of contractions was observed after oxytocin administration. These results support the idea that the uterus and fallopian tubes act as a peristaltic pump, which increases transport of sperm into the oviduct ipsilateral to the ovary bearing the dominant follicle. Oxytocin appears to play a critical role in this peristaltic pump. A failure of the peristaltic mechanism is possibly responsible for infertility. We propose the term tubal transport disorder (TTD) as a nosological entity. Results from HSS could be a useful adjunct for choosing treatment modalities in patients with patent fallopian tubes suffering from

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Ann. N.Y. Acad. Sci. 1101: 1–20 (2007). © 2007 New York Academy of Sciences.
doi: 10.1196/annals.1389.032

infertility. These patients may be better served with *in vitro* fertilization (IVF).

KEYWORDS: sperm transport; female genital tract; hysterosalpingoscintigraphy; intrauterine pressure; oxytocin; infertility

INTRODUCTION

One of the critical steps in the process of reproduction is the transport of spermatozoa from the vagina to the pars ampullaris of the fallopian tube. Its successful completion requires a mechanical patency as well as a functional integrity of the uterus and the oviducts.^{1,2} The biological significance and pathophysiology of transport function, in contrast to simple mechanical patency of the female genital tract, have also not been completely understood. The procedures used for clinical evaluation of the uterus and oviduct, that is, hysterosalpingography (HSG), hysterosalpingocontrastultrasonography (HyCoSy), and laparoscopy with chromopertubation (LSCP) are based on the infusion of liquid media into the uterus, such as a radiological water-soluble contrast medium, a contrast medium developed for ultrasonography and a solution of methylene-blue during laparoscopy, using pressure to force their passage through the fallopian tubes into the abdominal cavity, and mainly assess mechanical patency.³⁻⁵ Mechanical patency does not necessarily equate with functional integrity. Up to now, development and clinical application of methods for the assessment of functional aspects of the genital tract with regard to transport processes have not been available and thus not examined as possible diagnostic tools. By studying aspects of transport mechanisms in the uterus and the fallopian tubes through the use of hysterosalpingoscintigraphy (HSS), in conjunction with other biophysical and pharmacological interventions, we offer new insights into the pathophysiology of the female reproductive tract. Consequently, we suggest that tubal transport disorders (TTD), which can be diagnosed by HSS, may represent a thus far unrecognized factor in infertility.

METHODS

Patients

We reviewed the results of HSS in more than 1,000 women, ages 20–46, suffering from primary or secondary infertility of various etiologies, who underwent HSS followed by HyCoSy, to evaluate uterine and fallopian tube function. These women also underwent other diagnostic procedures, such as cycle monitoring combining determination of luteinizing hormone (LH), estradiol (E2), and progesterone in serum with sonographic determination of follicular development. Informed consent was obtained from all participants.

Materials

Urinary silastic catheters 6 or 8 charriere for intrauterine application of contrast medium fitted with an inflatable balloon were used (Uromed Kurt Dews GmbH, Oststeinbeck, Germany). We prepared the recording electrodes for electrohysterography using cephalic electrodes from Hewlett Packard Medical Products Group, Waltham MA, USA. Silastic, polyethylene, and teflon tubing was obtained from Reichelt Chemietechnik, Heidelberg, Germany.

Cycle Monitoring

We defined a dominant follicle as a follicle with a diameter of more than 10 mm and determined LH, E2, and progesterone in blood samples collected once daily starting on day 10 of the cycle using commercially available immunoassays (Boehringer Mannheim, Germany). The luteal phase was assessed by progesterone levels taken every 2–5 days during the 2 weeks after the beginning of the LH surge until the onset of menstruation. Ultrasonography was used to monitor follicular development using Siemens Sonoline AC and Siemens Versa Pro ultrasound devices (Siemens AG, Erlangen, Germany), both equipped with 5.0–7.5 MHz vaginal probes.

HSS

HSS was performed in the follicular phase of the cycle in 1,000 patients. Fifteen patients were examined inadvertently during the early- to midluteal phase. The largest follicle was identified by ultrasonography on the day of examination and its localization (left or right ovary) and diameter were determined. Using a catheter we applied 10 ± 2 MBq-TC-99 m labeled macroaggregates of human serum albumin (SolcoMAA, Solco Basel AG, Birsfelden Switzerland) with a size of 5–20 Hm, corresponding roughly to the size of spermatozoa, in a volume of 1–2 mL to the posterior vaginal fornix with the patient in a supine position. Scans with a gamma camera were obtained immediately after application and at various time intervals for up to 4 h, as already described.^{6,7} Color printouts of the scans were used for evaluation. A small mark was set on the skin between symphysis pubis and the umbilicus for topographical identification. The results were rated as (a) radioactivity within the cavum uteri, (b) radioactivity within the fallopian tubes, and (c) radioactivity within the abdominal cavity. Combining the examination with the findings obtained by ultrasonography, the results were further classified as ipsilateral when radioactivity concentrated predominantly within the fallopian tube on the side of the dominant follicle, as contralateral when radioactivity was detected predominantly in the tube opposite to the side of the dominant follicle,

as bilateral when activity was found equally distributed within both tubes, and as unilateral when activity was found within one tube only, but no dominant follicle was identified by ultrasound.

Validation of HSS

A bladder catheter was placed into the uterus in 4 patients after the examination was completed and flushed with 3 mL of saline to ascertain that the labeled material had remained in an intrauterine or intratubal position. The amount of radioactivity in the region of the uterus was determined and compared to that in the abdominal cavity by taking an additional scan after flushing. In addition, fluid was collected from the pouch of Douglas in 3 patients who underwent laparoscopy on the HSS day and the radioactivity of the fluid was counted in a well-type gamma counter. The fluid was divided into two aliquots. One aliquot (0.5 mL) was mixed with 3 mL 20% trichloroacetic acid. The sample was centrifuged, the supernatant removed, and the radioactivity in the precipitate was counted. The second aliquot was centrifuged, the pellet washed once with saline and counted after recentrifugation for 10 min. Microscopic examination of the pellet was done.

Effects of Oxytocin

The transport of radiolabeled microspheres was used to examine the effects of oxytocin in 50 patients, using serial HSS scans. The first scan was performed immediately after application of the microspheres to the vagina, followed 8–10 min later by a second scan. After intravenous (i.v.) administration of 3 international units (IU) oxytocin (Syntocinon, Sandoz AG, Nürnberg, Germany), two additional scans were taken, one immediately after oxytocin injection and the second scan 8–10 min later. Regions of interest (ROI) were placed for quantitative evaluation on both sides of the uterus in the area of the fallopian tubes and the radioactivity per unit time within these areas was recorded and plotted.

Measurement of Intrauterine Pressure (Hysterotonography)

During the follicular phase of the cycle, the intrauterine pressure was recorded in 25 patients using either a catheter fitted with two Millar-microtip transducers positioned 6 cm apart or with two catheters filled with sterile water, each connected to a Gould–Statham element as pressure recorder. The catheters were made from teflon or polypropylene tubing with an outer diameter of 1 mm and fitted at the tip with a small, inflatable rubber balloon as pressure

sensor (Hugo Sachs Elektronik, March-Hugstetten, Germany). The catheters were placed under ultrasonographic guidance into the uterus with the tip of the first catheter at the fundus (position I), and the tip of the second catheter just behind the internal os (position II). The catheters were either connected with an 8-charriere bladder catheter that could be blocked by an inflatable balloon or held in place by a wire clip attached to the cervix, so that their expulsion could be avoided. Using this multichannel recorder, the differential between the pressure measured at positions I and II (intrauterine pressure) was recorded for 10 to 20 min. Oxytocin was administered either i.v. (3 IU) or as nasal spray (4 IU) and recording continued for another 10 to 20 min. Frequency and amplitude of contractions and the pressure gradients between fundus and cervix uteri were determined using calipers.

Electrohysterography

Two silver electrodes made from a cephalic electrode were used for recording uterine electrical activity in 20 patients. The wires were immersed repeatedly into a solution prepared by mixing 1 mL medical grade silastic adhesive with 5 mL n-Hexane and allowed to dry at room temperature under a light stream of air for insulation. The insulating silastic layer was then removed carefully with a scalpel at a length of 2 mm from the tip of the wires. By placing one electrode into the fundus uteri and fixing the second one at the external os or within the cervix, we could measure electrical potentials continuously and record them with a Biofeedback system (SOM Biofeedback, Murrhardt, Germany) connected to a computer. A computer program adapted from a program for detection of pulses of hormones in plasma⁸ identified the amplitude and frequency of spikes and calculated the variability from point to point.

Doppler Ultrasonography of the Fallopian Tubes

Performing Doppler ultrasonography in 60 patients who underwent HyCoSy was used to determine flow through the fallopian tubes. We infused contrast medium (Echovist 300, Schering AG, Berlin, Germany) into the uterus via a catheter until the uterine cavity and the fallopian tubes could be visualized either by vaginal or by abdominal ultrasonography. After removal of the catheter, a pulsed Doppler beam was directed to the cavity uteri and the fallopian tubes. The ultrasound probe was held in place by a clamp fitted to a colposcope holder. Oxytocin was administered i.v. or intranasally at doses of 4 and 3 IU per application, respectively, after 2–5 min and the recording of Doppler signals was continued. A video printer was used during the recording periods. An increase to at least 10 cm/sec for a duration of at least 1 sec was defined as a signal. Frequency and intensity of the signals on the printout were determined using mechanical calipers.

Measurement of Ciliary Beat Frequency

Using a photoelectric technique and fast Fourier transform analysis, we determined the baseline ciliary beat frequency (CBF) of fimbria under standardized temperature conditions. Fimbrial portions of fallopian tubes were collected from 21 patients undergoing post partum sterilization, after obtaining written informed consent and local ethical committee approval. All study subjects had regular menstrual cycles before gravidity and no subject had used hormonal medications during pregnancy. Normal appearing, representative sections of fimbrial tissues, 0.5–1 cm in length, of both fallopian tubes of each subject were rinsed several times to remove all visible evidence of blood. Changes in CBF were documented by ROI measures for temperatures ranging from 37–39°C.

Clinical Evaluation of Tubal Patency

The mechanical tubal patency is defined as the observation of flow into the abdomen revealed by one of the following methods: HSG, HyCoSy, or LSCP. HSG was performed with a Schultze apparatus applied to the cervix for instillation of a radiological water-soluble contrast medium into the uterus (Isovist 300, Schering AG, Berlin, Germany). During HyCoSy a bladder catheter (Kinder- Ballon-Katheter 6 charriere, Uromed) was placed into the uterus and blocked; 2–4 mL of contrast medium developed for ultrasonography (Echovist 300, Schering AG, Berlin, Germany) was infused via the catheter into the uterus. The flow into the uterine cavity and the fallopian tubes was monitored by vaginal ultrasonography. Chromopertubation during laparoscopy was performed by placing a portio adapter into the uterus and infusing a solution of methylene-blue, with visualization of contrast escaping the fimbria as evidence of patency.

Statistical Analysis

The SPSS software package versions 6.1.3–11.00 were used for statistical analysis. Multiple data sets were analyzed by analysis of variance (ANOVA) followed by the Newman–Keuls test for comparing means. The level of significance was set as $P \leq 0.05$. Chi-squared analysis was used for testing distributions. Paired t -test was used when the effects of treatment were compared.⁹

RESULTS

Rapid transport of the microspheres from the vagina into the uterine cavity was confirmed by the detection of labeled particles in the uterus at the time of

the first HSS scan, as early as 2 min after intravaginal application. Uptake into the uterus was observed during the follicular as well as during the luteal phases of the cycle in every patient examined. Radioactivity entered the fallopian tubes either on both sides (15%) or on only one side (64%) in 79% of the patients studied during the follicular phase. In the remaining patients, radioactivity was detected only in the uterine cavity and did not migrate into the fallopian tubes. FIGURE 1 shows typical examples of the scans. Significant radioactivity entering the pelvis was observed in only 6% of the patients.

The ascension of radioactive particles into the uterus in the 15 patients examined during the luteal phase appeared to be indistinguishable from that observed during the follicular phase. However, we did not observe transport into the oviducts in any of the patients examined during the luteal phase. In addition, in these 10 women, we observed a qualitatively different pattern of distribution of radioactivity within the uterus compared to that observed during the follicular phase of the cycle. A rather broad area of radioactivity was observed during the luteal phase giving the impression of a large cavum uteri, while during the follicular phase, the area of maximal activity had an elongated shape.

Radioactivity from the uterine cavity and the oviducts was completely dispersed by flushing the uterus with a small volume of saline (~ 3 mL). In addition, more than 90% of radioactivity in the fluid collected from the cul de sac in 3 patients who underwent laparoscopy was found in the pellet after centrifugation and could be precipitated by trichloroacetic acid, indicating that most of the radioactivity was still protein bound.

FIGURE 2 shows the relationship between ipsilateral and bilateral entry of radioactivity into the fallopian tubes and the size of the dominant follicle. The frequency of ipsilateral transport of activity into the oviduct was found to increase from 10% to 75% with increasing diameter of the leading follicle,

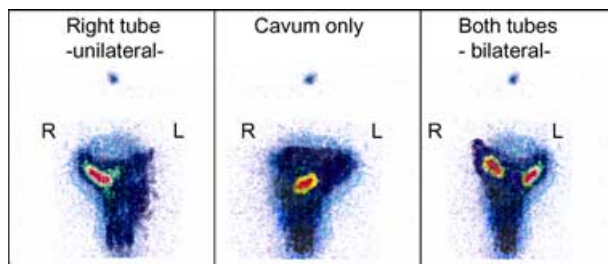


FIGURE 1. Typical examples of scans taken 10–20 min after application of 10–12 MBq ^{99m}Tc labeled microspheres to the posterior vaginal fornix, demonstrating (from left to right) uptake into the uterus and unilateral transport to the right fallopian tube (A), uptake into the uterus only (B), and bilateral transport into the oviducts (C). A marker is placed at half distance between the symphysis and umbilicus (reprinted from Wildt *et al.*²⁷ with permission).

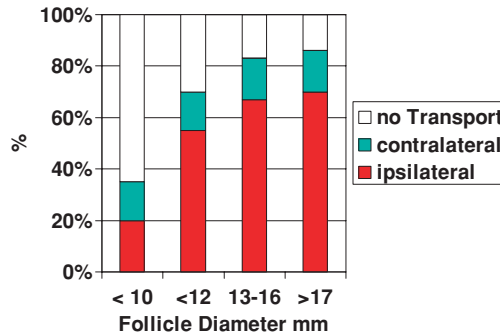


FIGURE 2. Lateralization of transport of labeled microspheres and size of the leading follicle. With increasing diameter of the dominant follicle, the proportion of patients exhibiting ipsilateral transport to the oviduct leading to the dominant follicle did increase progressively. The proportion of patients who had ipsilateral transport was higher in those who became pregnant after timed intercourse or intrauterine insemination than in those who did not conceive after this treatment (Treatment duration lasting up to 6 cycles). Up to a follicle size of 13 mm, ipsilateral transport could be diagnosed only in retrospect, at the time when a dominant follicle appeared on the side where radioactivity was concentrated.

when all patients were included in the analysis. The percentage of patients with ipsilateral transport was higher and increased from 25% to 95%, when only those patients were considered who later became pregnant either spontaneously or after intrauterine insemination.

TABLE 1 shows the relationship between the outcome of treatment of infertility and the asymmetrical distribution of radioactivity. The combined pregnancy rate for spontaneous pregnancies (Sp) or pregnancies following intrauterine insemination (IUI) in women exhibiting ipsilateral transport was 21.7%; when no entry of radioactivity into the tubes was found, the pregnancy rate was only 2% ($P < 0.05$). In contrast, no significant difference in pregnancy rate (22.7% vs. 24.5%, respectively) could be observed between both groups of patients who underwent *in vitro* fertilization (IVF) or intracytoplasmic sperm injection (ICSI).

The effects of oxytocin administration on transport of radioactivity are shown in FIGURES 3 AND 4. After oxytocin administration, radioactivity within

TABLE 1. Relationship between the outcome of treatment for infertility and the symmetrical distribution of radioactivity

	Ipsilateral Transport	No Transport
Pregnant (Sp* + IUI)	78/360 (21.7 %)	4/200 (2%)
Pregnant ** (IVF+ICSI)	25/110 (22.7%)	48/196 (24.5%)

*includes pregnancies after normal and timed intercourse.

**includes pregnancies after transfer of cryopreserved pronucleus cells.

the ROI on the ipsilateral side immediately increased, suggesting an increase in the amount of particles transported as a consequence of the administration of the peptide, as shown in FIGURE 3. Radioactivity on the contralateral side, in contrast, did not exhibit dramatic changes. FIGURE 4 summarizes the data for all 50 patients studied. During the luteal phase, oxytocin had no effect on the distribution of radioactivity within the uterus.

Doppler ultrasonography of the uterus and the oviduct filled with contrast medium resulted in eddy formations, indicative of turbulent rather than laminar flow within the tubes. Oxytocin administration resulted in an increase of turbulent flow, as shown in FIGURE 5, but only within the oviduct on the side of the dominant follicle. Only few signals could be detected on the contralateral side before and after the administration of oxytocin.

FIGURE 6 shows the results of the recording of the intrauterine pressure during the follicular phase of the cycle before and after oxytocin administration. Basal pressure increased significantly ($P < 0.05$) immediately following the administration of oxytocin.

FIGURE 7 shows the results of the recording of the CBF under a constant physiological temperature of 37°C. The mean (\pm SD) baseline in tubal explants

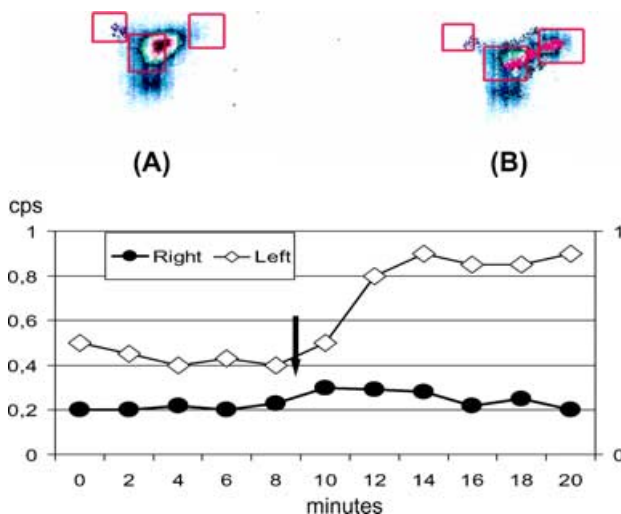


FIGURE 3. Intravenous (i.v.) administration of oxytocin (3 IU) in a patient during HSS. The upper panel (A and B) shows two scans taken 10 min apart, with the regions of interest (ROI) depicted as boxes over the cavum and the left and right oviducts, respectively. The lower panel shows radioactivity measured within the ROIs over the left and right oviducts and expressed as counts per second. The dominant follicle in this patient was located in the left ovary. Activity on the left side is higher than on the right side. The arrow marks the time when oxytocin was administered; this was followed by an increase of radioactivity found within the ROI on the left side, indicating increased transport into the left oviduct (reprinted from Wildt *et al.*²⁷ with permission).

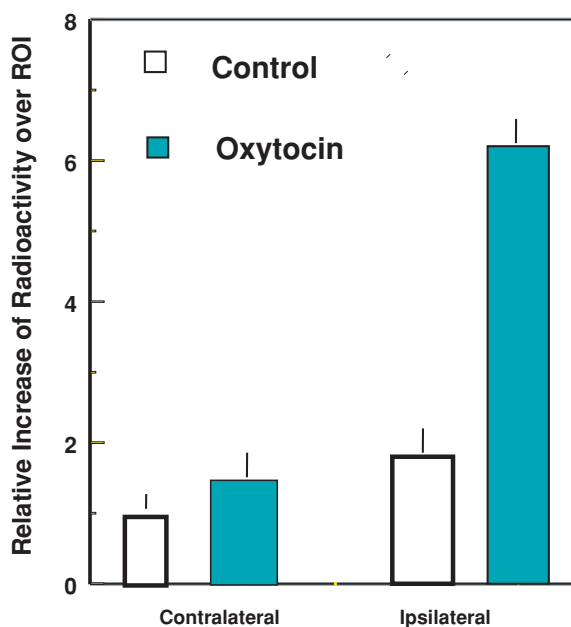


FIGURE 4. Relative increase of the radioactivity detected within the ROI placed over uterus and the fallopian tube leading to the dominant follicle. There is a significant ($P \leq 0.05$) increase in radioactivity immediately after oxytocin administration on the dominant, but not at the contralateral side. Data represent mean \pm SD of 50 observations (reprinted from Wildt *et al.*²⁷ with permission).

of the study population was 7.5 ± 0.5 Hz. A significant increase of CBF of 20% (9.5 ± 0.5 Hz) ($P < 0.05$) was recorded after the temperature increased from 37°C to 39°C .

DISCUSSION

Male germ cells have to migrate from the posterior vaginal fornix to the pars ampullaris of the fallopian tubes to fertilize an oocyte; the fertilized oocyte then has to be transported to the uterine cavity for implantation. The mechanisms and timing of this bidirectional travel are not completely understood. We studied the migration of radiolabeled immotile aggregates of serum albumin, used as surrogates for spermatozoa, from the vagina through the genital tract and explored some of the factors affecting this migration. We provide evidence that upstream transport in the genital tract may be composed of two components: a rapid uptake by the uterus from the vagina and a directed transport from the uterus to the oviduct toward the ovary bearing the dominant follicle. The former is observed during the follicular and luteal phase of the cycle, while

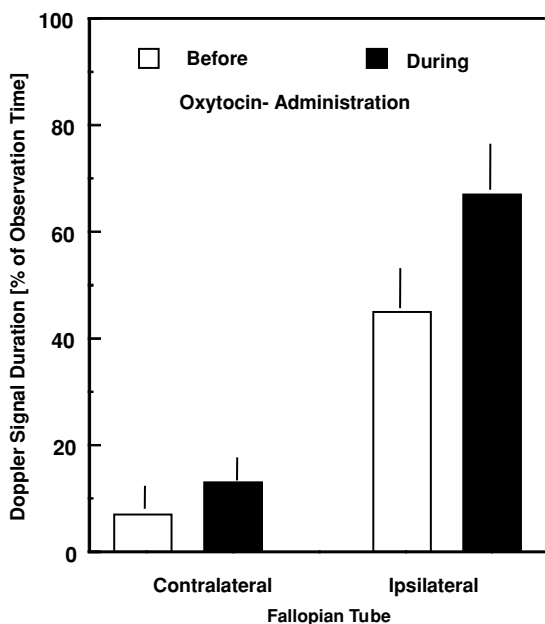


FIGURE 5. Doppler ultrasonography of the left and right fallopian tubes following instillation of echogenic contrast medium before and after oxytocin administration, demonstrating a significant increase ($P \leq 0.05$) in signal density and frequency after administration of the hormone. Data represent mean \pm SD of 30 observations (reprinted from Wildt *et al.*²⁷ with permission).

the latter is restricted to the follicular and preovulatory phase, becoming more prominent when the size of the leading follicle increases. Therefore, we believe that the ovary bearing the dominant follicle controls this directed transport.

All examined patients exhibited an uptake of the radiolabeled aggregates by the uterus. This is an indication that this part of the transport mechanism is rather stable and that inhibition of sperm uptake does not represent a major factor in infertility. The observation of this uptake into the uterus during the luteal phase of the cycle was rather unexpected because of the hypothesis that the cervical mucus becomes impenetrable for spermatozoa under the influence of elevated progesterone serum levels. Spermatozoa have previously been shown to be immotile in luteal phase mucus *in vivo* and *in vitro*, resulting in a failure to penetrate cervical mucus *in vitro* experiments.¹⁰⁻¹³ Our results may indicate that this does not necessarily affect that passive transport of spermatozoa, which may not be blocked during the luteal phase. Similar numbers of motile spermatozoa are found within the oviduct during the luteal as in the early- to midfollicular phase of the cycle, as previously reported by studies that examined the presence of spermatozoa in different compartments of the genital tract after intercourse. Nevertheless, the highest number of spermatozoa

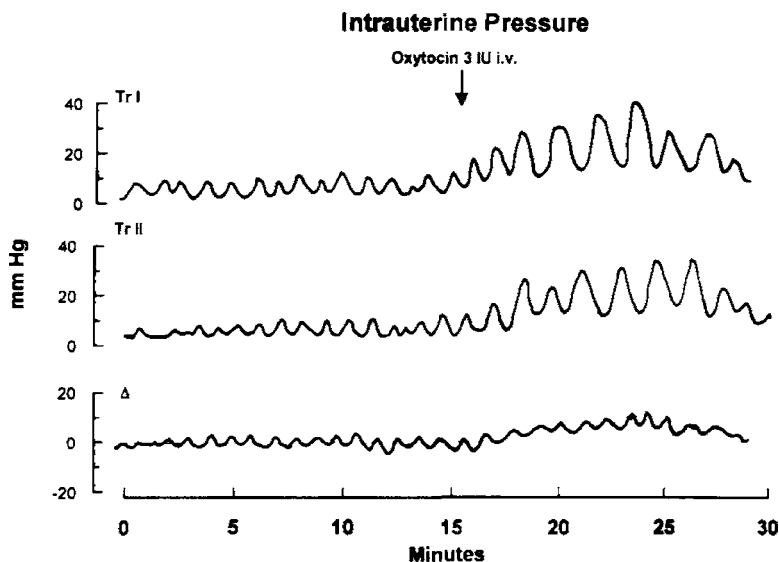


FIGURE 6. Intrauterine pressure recorded during the follicular phase of the cycle before and after the i.v. administration of 3 IU oxytocin. Transducer I (TrI) was placed in the fundal part (A), transducer II (TrII) near the internal cervical os (B). The arithmetic difference between pressure recorded in position II and the pressure recorded in position I is plotted in the lowest panel (C). Note the increase in basal tonus and the increase of the pressure difference between the two recording sites after oxytocin administration. The effect of oxytocin lasted for 20–40 min (reprinted from Wildt *et al.*, 1998²⁷ with permission).

can be detected in the fallopian tube during the preovulatory phase.^{10–14} With regard to sperm transport, our interpretation of the results of HSS is based on the assumptions that the properties of the labeled material used for examination are similar to those of human spermatozoa and that there is no separation of label from the carrier *in vivo*. Various radiolabeled compounds have been used the past 30 years for radionuclide imaging of the female genital tract, including aggregates of human albumin, radioactive inert gases, and labeled spermatozoa.^{6,15–22} In this study, human serum albumin macroaggregates with Tc-99m attached to the protein by noncovalent binding were used as surrogates for spermatozoa. We feel that we can adequately confirm that the radioactivity was protein-bound because: (1) we observed the disappearance of the radioactivity from the uterus after flushing with saline and (2) the radioactivity collected from the cul de sac at laparoscopy could be precipitated completely by acid and still could be centrifuged down at low speed 4–7 h after application excluding uptake by the lymphatic system.

Although HSS has not been widely used, it is a technically very simple procedure with little discomfort to the patient, in contrast to HSG. There is an apparent discrepancy between the results of HSS and those obtained with HSG

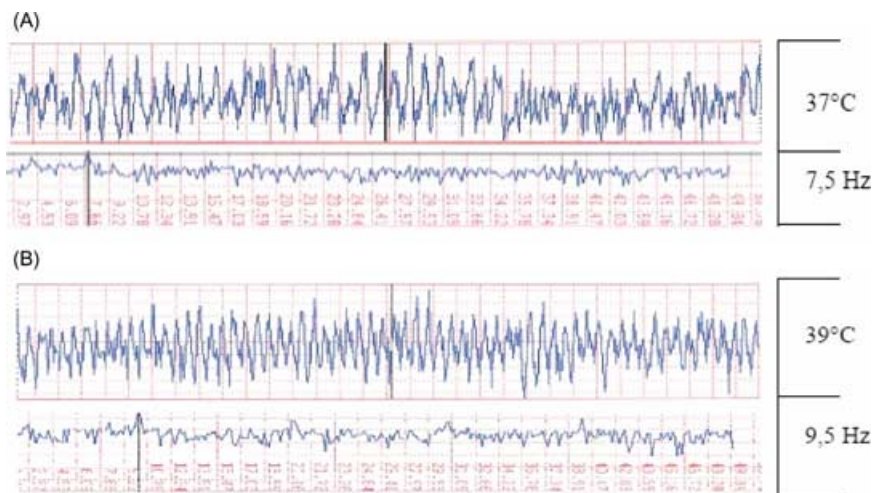


FIGURE 7. Ciliary beat frequency (CBF) is a local phenomenon in fimbrial cilia of human oviducts. Under physiological temperature conditions until 37°C, CBF is 7.5Hz \pm 0.5Hz (A). As temperature increased to 39°C, CBF increased exponentially up to 20% (9.5 \pm 0.5Hz, (B). A postovulatory increase of CBF in local areas of fimbrial cilia cells of the ipsilateral tube may guarantee the pickup of the oocyte-cumulus complex into the tube.

or laparoscopy; in the majority of patients with proven patency of both fallopian tubes only one oviduct could be visualized by HSS. The transport of the radiolabeled microspheres is physiologically restricted to the oviduct leading to the ovary bearing the dominant follicle while the contralateral fallopian tube appears to be functionally closed, as it is observed by a detailed analysis of the results of HSS and their correlation with the results of ultrasonography and determination of endocrine parameters for follicular growth.²³⁻²⁶ Our present study demonstrates that ipsilateral transport, as first shown by our group in 1992,²³ is a reflection of the physiological function of the uterus and the oviduct and not the consequence of tubal pathology or an artifact of the method. This demonstration is supported by the observation that the pregnancy rate after normal intercourse or intrauterine insemination was significantly higher in patients exhibiting ipsilateral transport than in those who did not.

Our results also imply that failure of transport in patients with otherwise mechanically patent fallopian tubes, may be considered an etiology of infertility. Most of the patients examined in this study would have been diagnosed as suffering from idiopathic infertility. We proposed the concept of TTD as a more adequate description of the condition of these patients.²⁷ The results of HSS may provide criteria for the choice of the adequate therapy in such women, since pregnancy rates in patients with TTD, which are extremely low following insemination or timed intercourse, can be increased substantially by *in vitro* fertilization.

The ovary bearing the dominant follicle appears to control the transport from the uterus to the oviduct. The proportion of patients exhibiting ipsilateral transport increased with the size of the dominant follicle, reaching up to 90% of those patients who became pregnant when the follicle diameter was 19 mm or more. The forces that are driving transport and the mechanisms directing this process need to be defined. Since the particles used for HSS are protein aggregates devoid of motility, motility of the spermatozoa can be excluded. Movements of the ciliae within the oviduct do not seem to be a major factor in rapid transport, since the beat of ciliae is directed from the ampulla to the uterus (the opposite direction), and women with Kartagener Syndrome, that is, congenital absence of ciliae, have no difficulties in becoming pregnant.^{1,28-31} It is also unlikely that capillary forces generated within the mucus and a difference in hydrostatic pressure between vagina and peritoneal cavity account for the immediate uptake from the vagina and the directed transport.³² Peristaltic contractions of the uterus and of the muscular layers of the fallopian tubes therefore represent the most likely candidates responsible for the rapid transport phenomena. Using direct measurement of intrauterine pressure or vaginal ultrasonography combined with videocinematography during the follicular phase of the cycle, peristaltic contractions of the nonpregnant uterus have been described in women during the normal menstrual cycle as well as in women suffering from primary dysmenorrhea or in women with endometriosis.³³⁻³⁷ The contractions seem to occur with a frequency of 2–5 per min and to exhibit a characteristic pattern of propagation in healthy women, depending on the phase of the menstrual cycle. While a cervicofundal propagation of peristaltic waves was found during the preovulatory phase of the cycle, a fundocervical direction predominated in the early follicular phase.

The strong positive correlation between the temperature and the oocyte pick-up rate in the animaloviductal infundibulum is demonstrated by a linear regression.³⁸ Preovulatory temperature differences between the ampullary and isthmic portions of a single tube have been previously reported and thought to primarily reflect the extent and activity of the vascular and lymphatic beds in the oviduct tissues.³⁹⁻⁴¹ We found periovulatory temperature differences of up to 1.5 °C between the two oviducts measured *in vivo* during tubal catheterization in a small group of patients, temperature being higher within the oviduct leading to the ovary bearing the dominant follicle (Wildt *et al.* unpublished). Furthermore, we found an exponential increase in CBF in the range of physiological temperature. This is in accordance with the report of a significantly higher temperature in the ipsilateral tube corresponding to the dominant follicle compared to the contralateral side in human oviducts.⁴² Our data suggest that this difference in periovulatory temperature between the two fimbriae may be responsible for the increased CBF on the side ipsilateral to the dominant follicle, underlining the concept of the uterus consisting of two functionally different components.

A number of hormones and paracrine mediators, such as prostaglandins, vasopressin, oxytocin, and various peptides can induce uterine contractions.⁴³⁻⁴⁶ The administration of oxytocin during HSS was followed by a five- to seven-fold increase in the radioactivity detected in the oviduct ipsilateral to the dominant follicle; in addition, systemic administration of oxytocin increased the amplitude of contractions and reversed the pressure gradient from a fundocervical to a cervicofundal direction. Oxytocin is known to play an important role in eliciting contractions of the pregnant and nonpregnant uterus, while oxytocin receptors have been demonstrated in the nonpregnant uterus of human females and laboratory animals.^{43,47-50} Following vaginal distension and cervical stimulation during intercourse, oxytocin is released from the posterior lobe of the pituitary in response to tactile as well as emotional stimuli.^{32,51-55} Synthesis of oxytocin has also been demonstrated within the endometrium and the ovary, respectively.^{50,56-59} Knaus demonstrated that injections of posterior pituitary extract containing oxytocin promptly induced contractions of the nonpregnant human uterus during the follicular phase, but not after ovulation.⁶⁰ Our results show a striking effect of oxytocin on uterine transport mechanisms and are in agreement with the early observations of Knaus, demonstrating the absence of directed transport during the luteal phase.

The electrical activity as a response to the oxytocin administration corresponded to the increase of intrauterine pressure. In most instances, no direct relationship between contractions and electrical activity was found. Further studies are necessary to explore the correlation between electrical activity and intrauterine pressure and to examine the validity of recording electrical potentials for the assessment of uterine contractions.^{61,62} The Doppler ultrasonography after administration of ultrasound contrast medium supports the observation of ipsilateral transport into and within the oviduct during scintigraphy. An increase in turbulent flow within the fallopian tube is indicated by an increase in signal density that was consistently observed immediately after oxytocin administration, either i.v. or intranasally. The increase of flow could only be detected within the oviduct leading to the dominant follicle, which shows that transport occurred predominantly in this direction.^{27,63}

Although the overall increase in transport may be explained by the stimulatory action of oxytocin on myometrial contractions, additional mechanisms acting at the levels of uterus and oviduct, such as asymmetric distribution of oxytocin receptors or changes in the resistance of the oviducts caused by the activation or relaxation of smooth muscle cells at the uterotubal junction, are required to account for the unilateral transport. This question cannot be answered by the present studies. Therefore, we propose the following hypothesis, schematically depicted in FIGURE 8: (1) The fallopian tubes are functionally closed in the absence of ovarian hormones. (2) Hormones that cause relaxation of smooth muscle cells are produced by the ovary bearing the dominant follicle. (3) Unilateral transport is to be regarded as the consequence of active relaxation of the myometrium at the side of the ovary that is bearing the

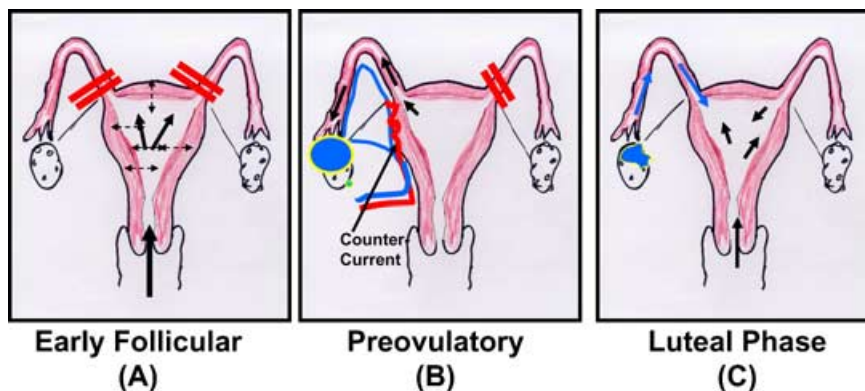


FIGURE 8. Schematic representation of the model of directed transport. During the early follicular phase (A) both fallopian tubes are functionally closed, transport occurs from the vagina to the uterine cavity. Contractions of the myometrium, indicated by the broken arrows, which are followed by relaxation, cause a negative pressure within the uterus when compared to the vagina. (B) The dominant follicle has been selected. Concentrations of progesterone, produced by the dominant follicle, are elevated at the uterotubal junction due to a countercurrent system indicated by the arrows, causing relaxation of the musculature. Since the contralateral side remains functionally closed, transport is directed into the fallopian tube at the side of the dominant follicle. (C) Demonstrates transport during the luteal phase of the cycle. Uptake into the uterus is not impaired, but transport into the fallopian tubes appears to be completely blocked. Transport of the fertilized oocyte is depicted by the arrows within the right fallopian tube, however, the mechanisms governing embryo transport remain to be elucidated.

dominant follicle rather than the induction of a contraction at the contralateral side.

Progesterone can also induce relaxation of the myometrium. The preovulatory follicle produces progesterone in increasing amounts. In addition, progesterone concentrations in the venous effluent from the ovary bearing the dominant follicle are higher than those from the contralateral ovary several days before ovulation.^{64,65} Progesterone could be delivered to the area of the uterotubal junction through the arteriovenous countercurrent exchange system that has been identified between the ovary and the uterus.⁶⁶⁻⁷⁰

In conclusion, our data demonstrate that the uterus and fallopian tubes seem to act as a functional unit and peristaltic pump that provides the pressure gradients necessary to transport spermatozoa from the vagina to the fallopian tubes. Secretory products originating from the ovary bearing the dominant follicle allow further transport to the ampullary part of the tube on the side of the follicle destined to ovulate, inducing the active relaxation of a functional sphincter mechanism located in the area of the uterotubal junction, while the contralateral oviduct remains functionally closed. Consequently, the probability for fertilization is increased by the maximized number of spermatozoa at

the site where the oocyte is released. Oxytocin contributes to the control of this process by activating pump mechanisms via contraction of uterine smooth muscles. Disturbance of these mechanisms interferes with tubal transport, causing infertility, even in the presence of mechanically open fallopian tubes. HSS appears to be a suitable method to diagnose this TTD.

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